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THIRD SERIES FOUNDED BY EDWARD JACKSON

CONTENTS

Vision in the animal world ..... *Sir Stewart Duke-Elder* 447
Photocoagulation of the retina ..... *DuPont Guerry, III, H. Wiesinger and W. T. Ham, Jr.* 463
Ocular toxoplasmosis ..... *Michael J. Hogan* 467
Adhesion of lens capsule ... *Algernon B. Reese and Joseph A. C. Wadsworth* 495
Aqueous humor dynamics ..... *Ahti H. A. Tarkkanen and Bernard Becker* 499
Primary tumors of the orbit .. *Virgil A. Beuerman and George L. Tabor, Jr.* 501
Exfoliation of the lens capsule ..... *Harold Gifford, Jr.* 508
Angiomatosis retinae ..... *Derrick Vail* 525
Implants of sclera ..... *H. H. Chi, C. C. Teng and H. M. Katzin* 534
Penetrating keratoplasty ..... *Brendan D. Leahey* 541
Surgery for macular degeneration ..... *Ronald M. Burnside* 584
Removing corneal-scleral sutures ..... *Albert C. Esposito* 587
White spots of the iris ..... *M. F. Mueller* 587
Moist chamber ..... *Lester L. Covell* 589
Corneal graft table ..... *Rudolph Bock* 591
Near-vision test card ..... *Arthur H. Keeney and H. Lyle Duerson, Jr.* 592
Supplemental intravenous analgesia ..... *Frederick D. Williams* 594
Anesthesia in rabbit surgery ..... *Wayne Collins, L. Byerly Holt and Kathryn Robson* 596

DEPARTMENTS

Society Proceedings 597 Correspondence ... 605 Abstracts 610
Editorials ..... 600 Book Reviews .... 605 News Items 633

For a complete table of contents see page xxvii

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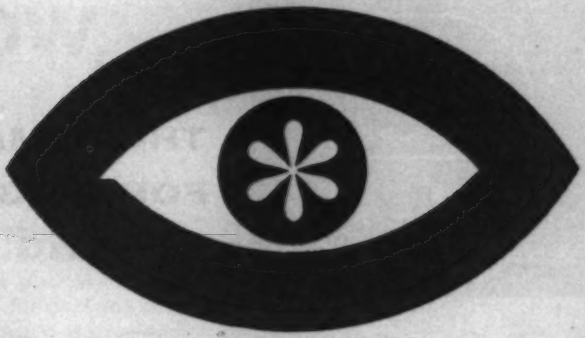

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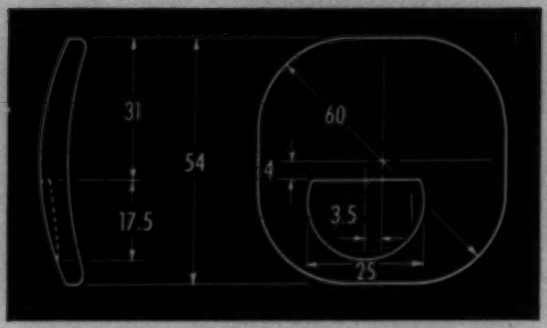

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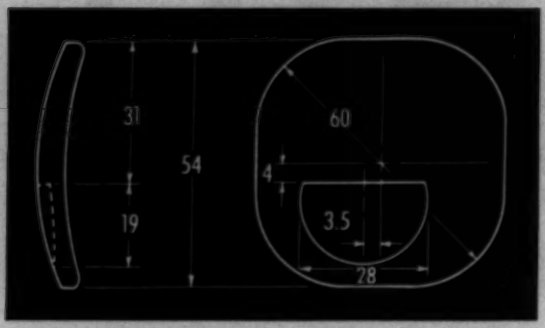

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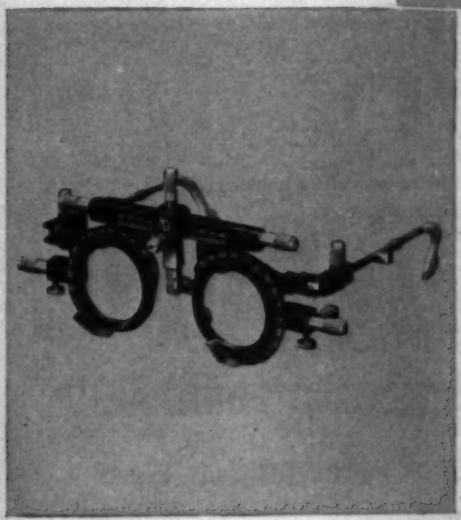

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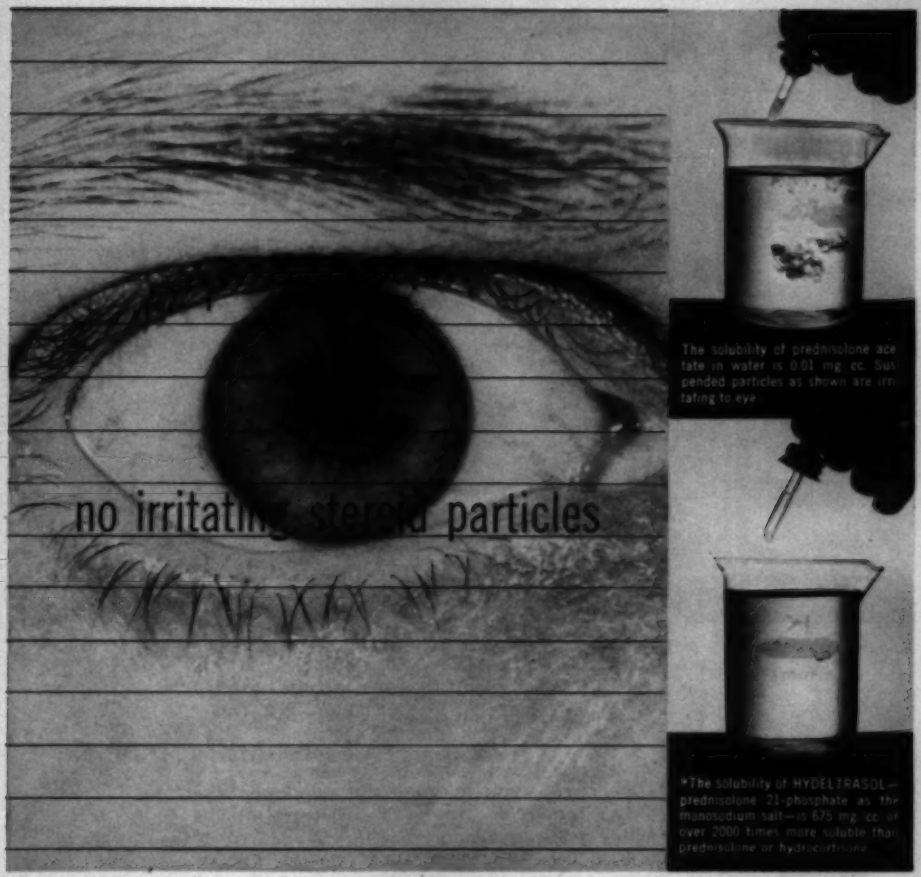
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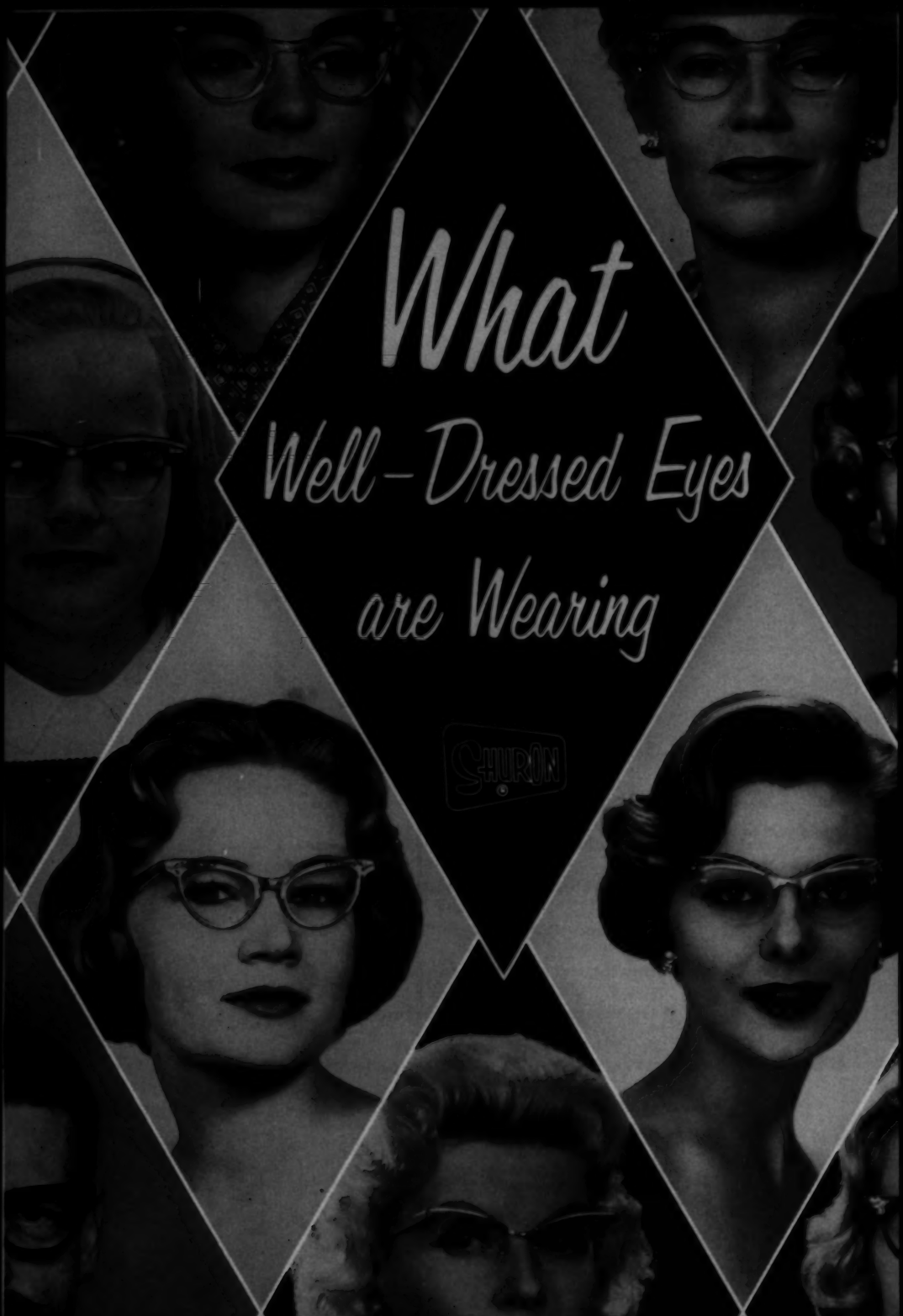
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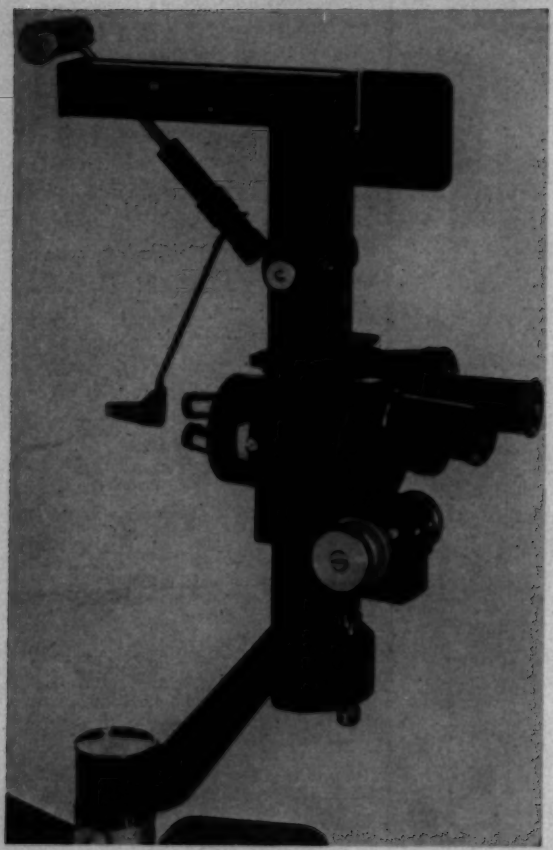

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(1) Leopold, I. H.: New York J. Med. *56*:2803, 1956. (2) King, J. H., Jr., and Weimer, J. R.: A.M.A. Arch. Ophth. *54*:46, 1955. (3) Gordon, D. M.: Am. J. Ophth. *41*:593, 1956. (4) King, J. H., Jr.; Passmore, J. W.; Skeehan, R. A., Jr., and Weimer, J. R.: Tr. Am. Acad. Ophth. *59*:759, 1955. (5) O'Rourke, J. F.; Iser, G., and Ryan, R. W.: A.M.A. Arch. Ophth. *55*:323, 1956. (6) Mosquera, J. M.: Día Méd. *28*:38, 1956.

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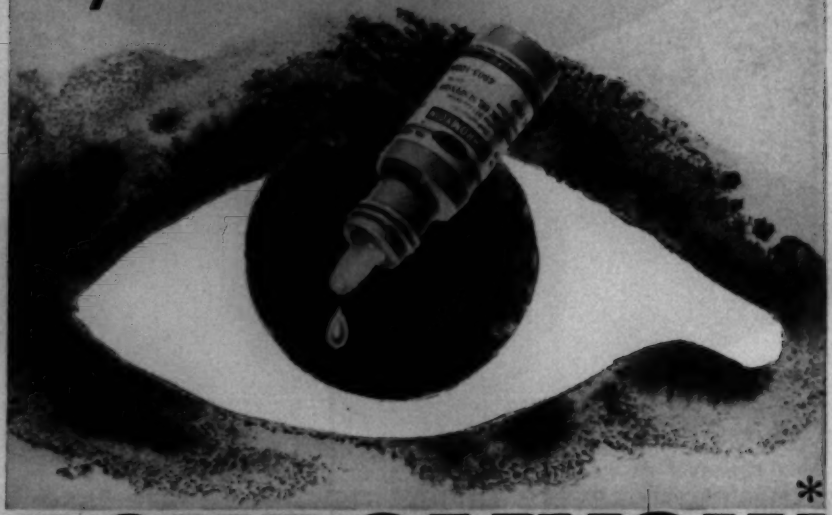

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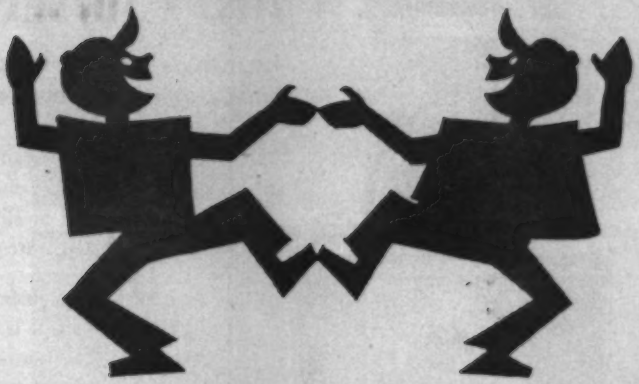
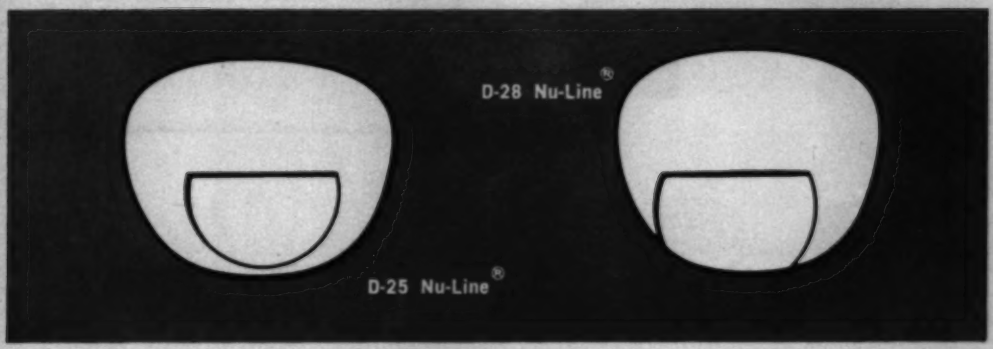


only the segment width changes



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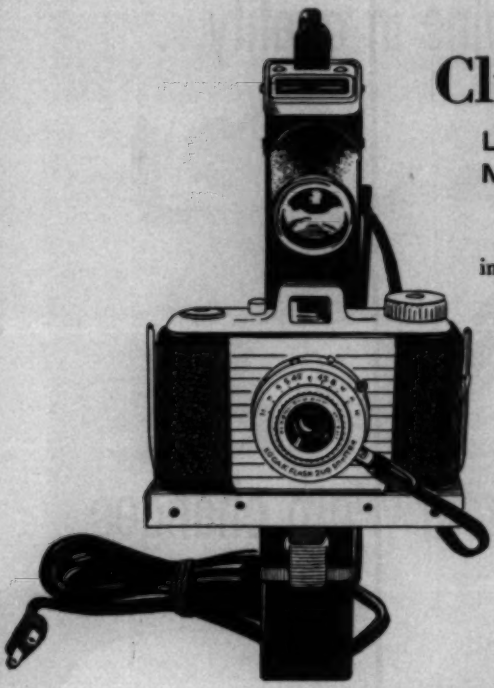

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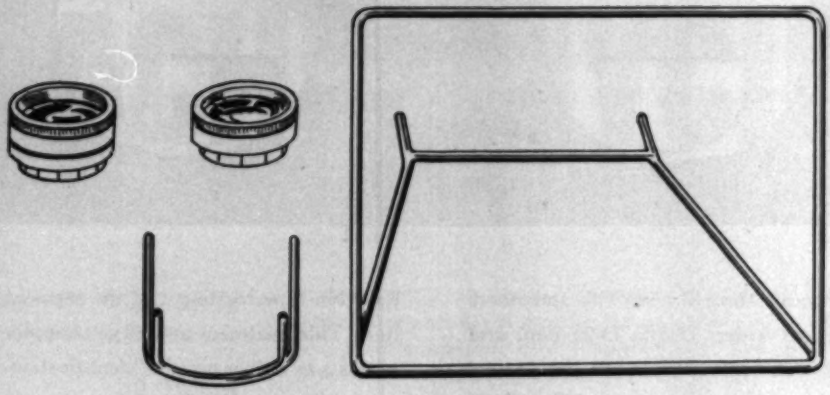

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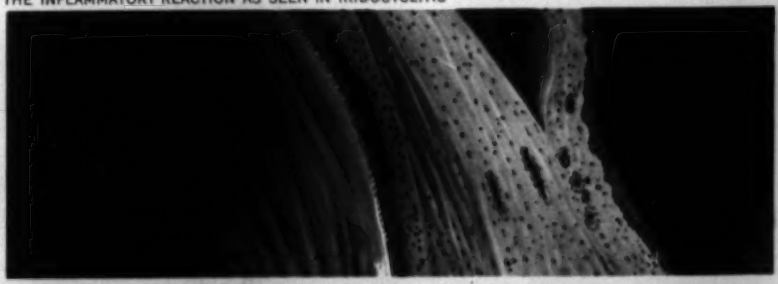
EXUDATIVE INFLAMMATION OF THE UVEAL TRACT

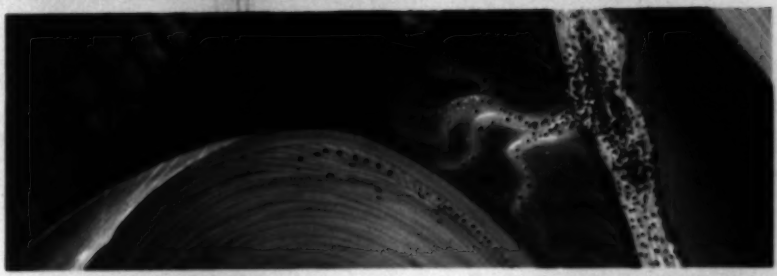
THE INFLAMMATORY REACTION AS SEEN IN IRIDOCYCLITIS

A. Normal tissue. From left to right: posterior surface of ciliary ring, ciliary retina, pigmented layer, ciliary muscle, sclera, and conjunctiva.

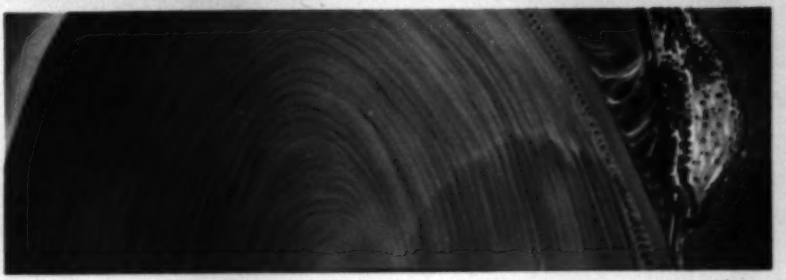


B. Hyperemia is the result of reaction to an endogenous toxin or allergen. Blood vessels are dilated. There is heightened local heat and color. Escape of blood plasma causes edema.

C. The next stage is that of exudation, shown here as macrophages and fibrin streaming from the posterior surface of the iris.



D. As the condition becomes subacute, there is concomitant active exudation and repair. With chronicity, fibroblasts proliferate, new capillaries develop, and various kinds of white cells appear. Formation of a posterior synechia is shown.



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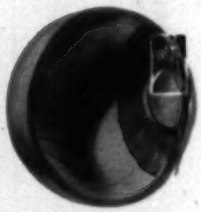
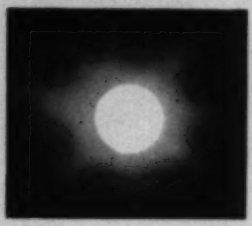


IN OCULAR INFLAMMATORY DISEASES Medrol

A SYNOPSIS OF OCULAR INFLAMMATORY DISEASE (IRIDOCYCLITIS)

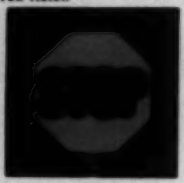
Subjective symptoms:

Photophobia

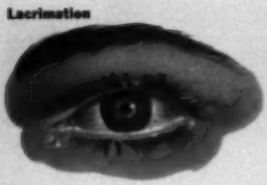


Trigeminal pain

Blurred vision



Lacrimation

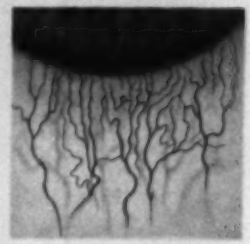


Clinical findings:

Hazy iris

Swollen upper lid

Ciliary injection

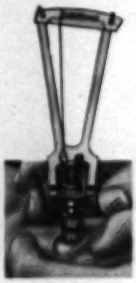


Sequelae: (if untreated)

Anterior and posterior synechiae

Lenticular changes

Secondary glaucoma



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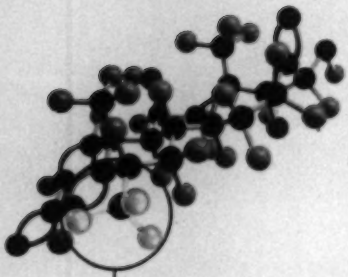

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1. Feinberg, S. E.: Medrol in Allergic Conditions: Clinical and Experimental Findings, Metabolism 7:477 (July) 1958.
2. Gordon, D. M.: Methylprednisolone in Ophthalmology, Metabolism 7:569 (July) 1958.

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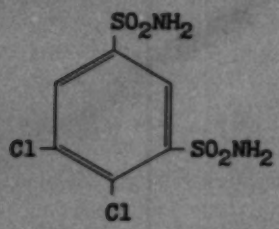
CHEMISTRY

'Daranide', a dichlorinated benzenedisulfonamide, is known chemically as 1,3-disulfamyl-4,5-dichlorobenzene and is designated by the generic name of dichlorphenamide. It has the following structure:



MODE OF ACTION

'Daranide' is primarily a carbonic anhydrase inhibitor; i.e., it interferes with the catalytic activity of this enzyme, which is concerned with the formation of H^+ and HCO_3^- ions and the conservation of base as sodium bicarbonate. Under the influence of 'Daranide' the renal excretion of sodium, potassium, and bicarbonate is increased and an alkaline urine is produced. However, this compound also has the

advantage of causing a definite increase in chloride excretion. Partially as a result of the greater excretion of chloride, 'Daranide' does not produce metabolic acidosis as readily as other compounds of this nature. Furthermore, in animal studies 'Daranide' has been shown to maintain its essential activity over the course of weeks or months.

The compound does not appear to be concentrated in gastric mucosa in sufficient amounts to influence materially the activity of carbonic anhydrase in this tissue. Thus, in dogs, gastric motility or secretion is not affected to any significant degree by the administration of 'Daranide'.

PHARMACOLOGY

'Daranide' is uniformly and well absorbed following its oral administration; it is essentially as active when given orally as parenterally. The enhancement of sodium, potassium, and chloride excretion by the oral administration of a single dose is rapidly manifested and persists for a number of hours, indicating a prolonged duration of action of the compound. The urinary pH is elevated as the result of sustained bicarbonate excretion. However, greater chloruresis and less acidosis are induced than with other carbonic anhydrase inhibitors, with consequent greater efficacy on repeated administration. The natriuretic effect of 'Daranide' has been observed even after 10 weeks of continued administration to dogs. The activity of 'Daranide' is not impaired in the presence of an acid urine such as that accompanying the administration of ammonium chloride.

'Daranide' has a low inherent toxicity when administered orally or parenterally to laboratory animals. The compound has been given orally to dogs and rats over a period of at

least six months with essentially no evidence of toxicity. Pharmacologic investigation indicates an absence of irritating effect on the mucosa of the eye as demonstrated by a lack of local anesthetic activity or irritation when a 1 per cent concentration of the drug (suspended in tragacanth) is instilled into the conjunctival sac of the rabbit eye.

CLINICAL EVALUATION

Effect on Intraocular Tension

Studies in humans have demonstrated that 'Daranide' administered orally reduces intraocular pressure in both glaucomatous and nonglaucomatous eyes. The onset of action following a single dose is within an hour and maximal effect is observed within two to four hours. The lowered intraocular tension is maintained for approximately six hours. It has been possible to control excessive intraocular pressure in patients with glaucoma for a period of many months by the daily combined use of 'Daranide' and miotics. Tonographic studies have shown that 'Daranide' lowers intraocular pressure by inhibiting the formation of aqueous humor in normal as well as in glaucomatous eyes.

Effect on Electrolytes

In the human as in the laboratory animal, 'Daranide' enhances the excretion of sodium, potassium, bicarbonate, and water. An increased chloride excretion greater than that following the use of other carbonic anhydrase inhibitors is also observed with 'Daranide'. This enhanced excretion of chloride explains, at least in part, the continued efficacy of 'Daranide' with repeated administration and the lesser propensity for the development of metabolic acidosis.

As is the case with all carbonic anhydrase inhibitors, 'Daranide' in high doses causes some

decrease in renal blood flow and glomerular filtration rate.

INDICATIONS

'Daranide' is indicated for oral treatment of various types of glaucoma:

chronic simple (wide angle) glaucoma
acute congestive (narrow angle) glaucoma
chronic congestive glaucoma
secondary glaucoma (acute phase)
preoperative control of intraocular tension of glaucoma

DOSAGE

The usual adult dosage range is from 25 to 50 mg. (½ to 1 tablet) once to three or four times daily. Dosage must be carefully adjusted to meet the requirements of the individual patient.

Therapy with 'Daranide' is usually most successful when employed in conjunction with miotics such as pilocarpine, physostigmine, 'Floropryl' (isoflurophate), or 'Carcholin' (carbachol). In acute congestive glaucoma, 'Daranide,' with miotics, should be administered promptly in an attempt to bring about rapid reduction of intraocular tension. If this is not quickly relieved, surgery may be mandatory. In chronic congestive glaucoma, surgery may be necessary if the intraocular tension is not brought successfully under control after an adequate trial period of therapy with 'Daranide'.

PRECAUTIONS

Since 'Daranide' is a carbonic anhydrase inhibitor, certain side effects characteristic of this class of compounds will occur, particularly in the higher dosage ranges. These effects may in-

clude anorexia, nausea, vomiting, nervousness, lassitude, depression, confusion, disorientation, sedation, dizziness, ataxia, tremor, tinnitus, paresthesias, and pruritus. Fortunately, the therapeutic amount of 'Daranide' required for most patients is well beneath the level that will produce these effects. When they do occur, reduction of dosage or temporary discontinuance of the drug is indicated.

It is essential to keep a close check on the electrolyte balance of the patient during therapy with 'Daranide', as with patients on any other carbonic anhydrase inhibitor.

SUPPLIED

'Daranide' Tablets, 50 mg., bottles of 100 and 1000.

REFERENCES

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Crosley, A.P., Jr., and Cullen, R.E.: Effects of Dichlorphenamide on Renal Hemodynamics and Electrolyte Excretion, Fed. Proc. 16: 289, March 1957.

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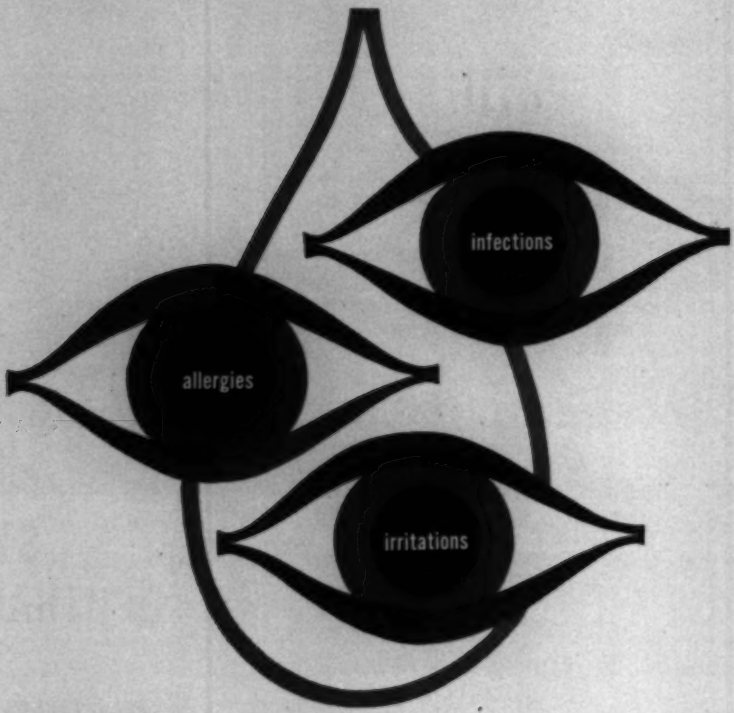

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(Figure 2)
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1. *Am. J. Ophth.* 42:771, 1956.
2. *Am. J. Digest. Dis.* 22:5, 1955.
3. *Med. Times* 84:741, 1956.

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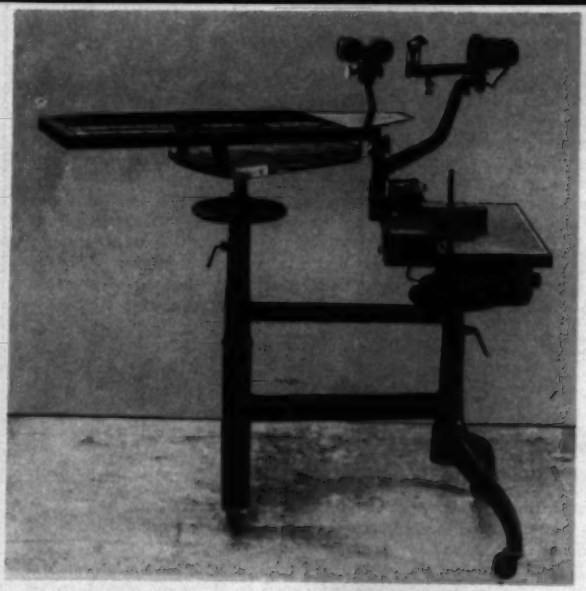

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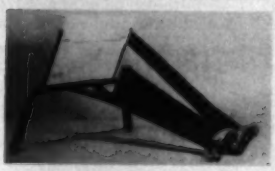

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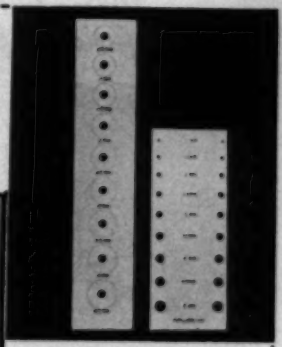
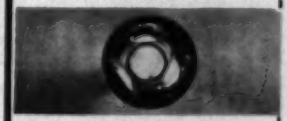
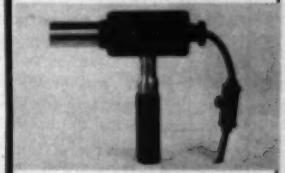


Keratometer Chart, #6510. Pupillometer Chart, #6511. Both are Otto Barkan charts by Parsons.



Goldmann 3-Mirror Lens, #6520. For examination on the angle and the periphery of the fundus while seated at the slit lamp.



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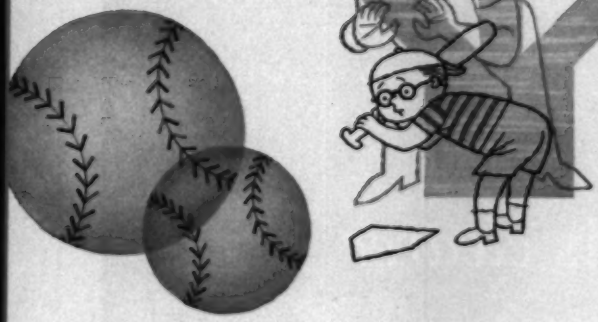

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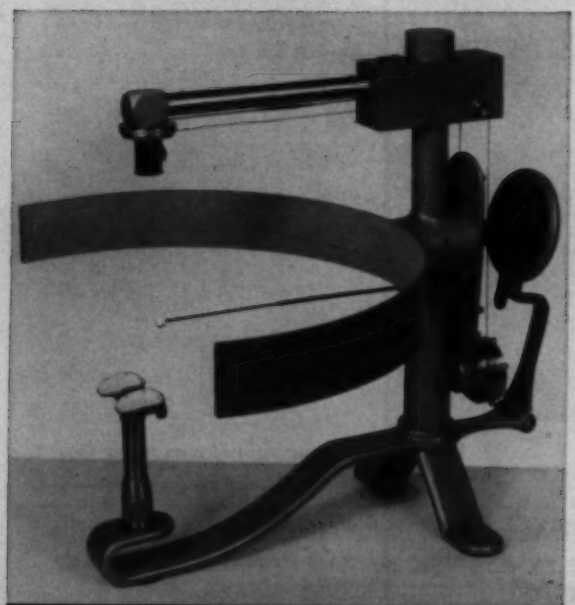

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CONTENTS

ORIGINAL ARTICLES

The emergence of vision in the animal world: The Lister Oration. Sir Stewart Duke-Elder .. 447
Photocoagulation of the retina: Report of a successfully treated case of angiomatosis retinae. DuPont Guerry, III, H. Wiesinger, and W. T. Ham, Jr. 463
Ocular toxoplasmosis: The XIV Jackson Memorial Lecture. Michael J. Hogan 467
The adhesion of the lens capsule to the hyaloid membrane: And its relation to intracapsular cataract extraction. Algernon B. Reese and Joseph A. C. Wadsworth 495
Aqueous humor dynamics: The effect of pentolinium (Ansolysen) on normal human eyes. Ahti H. A. Tarkkanen and Bernard Becker 499
Primary tumors of the orbit: With case reports. Virgil A. Beuerman and George L. Tabor, Jr. 501
A clinical and pathologic study of exfoliation of the lens capsule. Harold Gifford, Jr. 508
Angiomatosis retinae, eleven years after diathermy coagulation. Derrick Vail 525
Experimental implants of sclera into the anterior chamber. H. H. Chi, C. C. Teng and H. M. Katzin 534
Penetrating keratoplasty: Observations based on a series of 148 cases with special emphasis on techniques of graft fixation. Brendan D. Leahey 541
Surgery for senile macular degeneration. Ronald M. Burnside 584

NOTES, CASES, INSTRUMENTS

DeWecker scissors: In removing corneal-scleral sutures. Albert C. Esposito 587
White spots of the iris. M. F. Mueller 587
Moist chamber. Lester L. Covell 589
Corneal graft table. Rudolph Bock 591
Collated near-vision test card. Arthur H. Keeney and H. Lyle Duerson, Jr. 592
Supplemental intravenous analgesia: For cataract surgery. Frederick D. Williams 594
Tubocurarine and Nembutal anesthesia: In rabbit eye surgery. Wayne Collins, L. Byerly Holt and Kathryn Robeson 596

SOCIETY PROCEEDINGS

New England Ophthalmological Society, November 20, 1957 597
College of Physicians of Philadelphia, Section on Ophthalmology, December 19, 1957 599

EDITORIALS

Prevention of angle-closure glaucoma 600
Italian ophthalmology 602

CORRESPONDENCE

Recollections of Lawrence T. Post 605

BOOK REVIEWS

Ophthalmic Plastic Surgery 605
Contributions to the History of Ophthalmology 606
Veterinary Ophthalmology 608
Chemistry and Biology of Mucopolysaccharides 608
The Evil Eye 608
Guide to Occupational and Other Visual Needs 609

ABSTRACTS

Anatomy, embryology, and comparative ophthalmology; General pathology, bacteriology, immunology; Vegetative physiology, biochemistry, pharmacology, toxicology; Physiologic optics, refraction, color vision; Diagnosis and therapy; Conjunctiva, cornea, sclera; Uvea, sympathetic disease, aqueous; Glaucoma and ocular tension; Crystalline lens; Retina and vitreous 610

NEWS ITEMS 633

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AMERICAN JOURNAL OF OPHTHALMOLOGY
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THE EMERGENCE OF VISION IN THE ANIMAL WORLD*

THE LISTER ORATION

SIR STEWART DUKE-ELDER
London, England

To be invited to give the Lister Oration is indeed a unique experience which comes once in a lifetime, and that to few. Like all experiences worth having, it is charged with emotion: at first a thrill of pride, for what surgeon—and of all surgeons what British surgeon; and of British surgeons, what surgeon trained in the Scottish universities where Lister did his essential work—could fail to be flattered that he had been chosen to keep that memory officially alive? But after pride the fall; for what orator, confronted with a task of such responsibility, could fail to be overwhelmed by a sense of inferiority? For today we commemorate the life's work and the character of a giant among men.

There have been indeed few men who have created a complete revolution in the philosophy and practice of the branch of knowledge to which they had dedicated themselves, who have thrown a bridge across a great divide on the way to understanding, that journey without end, so that men could say "this is indeed a new world" as surely as, on a greater and higher plane, the history of Christendom is divided into two epochs—before and after Christ. In such a way in cosmology, Copernicus, watching the heavens from the shores of the Baltic Sea, overturned the system of Aristotle and Ptolemy by transferring the center of the universe from the earth to the sun; in such a way in natural philosophy, Francis Bacon, in England, displaced the authoritative traditions of the classical scholars by stressing the importance of the experimental method in the acquirement of knowledge. Similarly in physics there was a pre-Newtonian and a Newtonian era; in biology a pre-Darwinian and a Darwinian; in medicine a pre-Harvean and a Harvean; and in surgery a pre-Listerian and a Listerian. It is curious, incidentally, how many of these revolutionaries were English.

In each case, each branch of knowledge had stood still since its first awakening in the river-civilizations of the Ancient World and its crystallization in the glory of classical Greece; in each case a prophet arose who, partly by the inspiration of that curious something we call genius, but largely by force of character and unremitting labor over many years, transformed a science by substituting for the sterility of the past a completely new vision for the future. Each of them had to fight a battle alone in the face of prejudice, ridicule, and often obloquy; but such glory as was theirs is not to be shared.

To this generation pre-Listerian surgery is a thing of history; none of us here has seen its horrors or experienced the revolution he accomplished. And so I think in this lecture, founded to commemorate his achievement, it is well to stop for one moment that we may remind ourselves of its greatness. It can truly be said that, before Lister, the results of surgery in the middle of the last century were little better than in the days of Hippocrates; probably in Lister's

* Delivered before the Royal College of Surgeons (London) March 28, 1958, and published in the *Annals of the Royal College of Surgeons.*

early days it was worse than it had ever been, partly because the recent introduction of anesthetics was tempting surgeons to undertake techniques which the unanesthetized patient could not tolerate, and partly because the industrial revolution had stimulated a remarkable increase in the population of these islands, particularly in the towns, so that in the cramped and insanitary hospitals the opportunities for cross-infection had increased manyfold. An operation was a procedure to be adopted only as a last desperate resort, for a pin-prick served as the gate of death; to open the abdomen, the chest, or the head was unthinkable. A surgical hospital was a charnel house from which only the fortunate few emerged.

That was pre-Listerian surgery. That today we can at leisure and almost with nonchalance explore every cavity and recess in the body, that our techniques are limited not by fear but by ingenuity, that today a hospital is a gate of hope, the cleanest and often the happiest place in a community—all that is due to Lister. By his work in his lifetime, and by the continuance and extension of his teaching after his death, he has eased more pain and suffering and saved more lives a thousand-fold, than have been lost in all the battles since there were records of war. Surely a legacy to mankind worthy of a commemorative lecture; but as surely an achievement to make any lecturer despair of doing it justice.

In view of the fact that Lister's great contributions to surgery and humanity stemmed from his capacity to see beyond the confines of the technical aspects of surgery to the new world of micro-organisms, at that time being brought to notice by Pasteur, so, instead of telling you of some of the technical aspects of my particular craft—and probably boring most of you thereby—I am going to ask you to explore with me the animal world. When, in 1877, Lister left Scotland to return to London to convert the English, all the surgical world assembled at Kings College for his inaugural lecture agog to hear —and certainly to criticize—the latest contribution to his new technique. But for some months previously, Lister had been interested in the curdling of milk, and instead of surgery he gave them a dissertation on the Bacillus lactis he had discovered, proving the part it played in this phenomenon.

I am therefore taking a leaf out of Lister's book and bringing you to a nonsurgical world—albeit a world full of interest and delight, and importance. It is indeed a fascinating subject—this story of how animals came to see; and then, having seen, of what they see; and, more intriguing still, of what they make of this world we share with them. And it is important; for the faculty of vision was probably the greatest single factor in the evolution of man. Although we are highly visual creatures, this does not apply to the lower animals. Most of them, indeed, depend primarily on other senses rather than on sight—initially, in the more primitive creatures, on the chemical and tactile senses, and in the later stages of evolution, on the extensions therefrom into the senses of smell and hearing.

In the lower vertebrates the sense of smell is the most fundamental sense and the forebrain has an olfactory function; vision is a subsidiary sense, relegated to a small and obscure place in the mid-brain (fig. 1). Not until mammals are reached is vision translated from the midbrain to the cerebral cortex, until in primates vision comes to dominate the entire brain with its receptive center behind, its wide contiguous association areas and its motor and co-ordinative regions flung forward in the frontal lobe, the seat of intelligence, close to the center for the control of the hands. In this way sensory reception becomes vision in thought and action, and the roving eyes and the exploring fingers could combine with intelligence to unravel the secrets of the world. It was this process of ousting the sense of smell as a primary determinant of behavior, this transfiguration of the nose-brain to the eye-brain, that constituted the greatest single factor in assur-

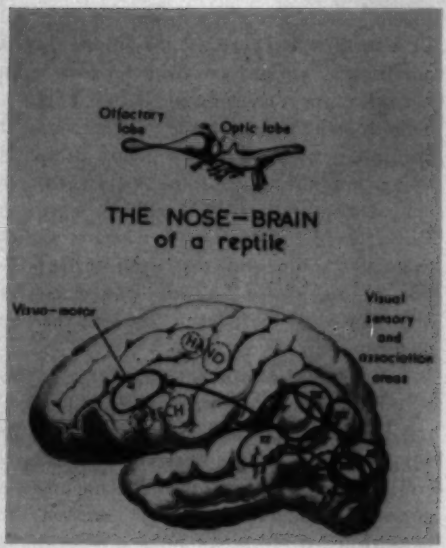

Fig. 1 (Duke-Elder). The nose-brain of a reptile and (below) the eye-brain of man.

ing the dominance of man and establishing his physical dexterity and his intellectual supremacy. This it was essentially that gave him power to attain new skills, and by opening up a fuller understanding and appreciation of the meaning of the outside world, it provided a potent stimulus for the fuller development of every part of the brain.

In an attempt to analyze the visual appreciation of animals, let us start where every schoolboy starts—with the lowly amoeba. In order to obtain a supply of fresh nourishment in the water wherein it lives, an amoeba periodically throws out pseudopodia, an activity due to physical changes in the gelation of its surface layer. If a pseudopod encounters something noxious, the surface layer gelates, the pseudopod stops, protoplasmic flow starts in the reverse direction and the amoeba travels away from an environment that is unsuited to it (fig. 2). This is effected by light. The same gelating effect on the surface layer is produced by mechanical stimulation, by chemical substances, or by heat; but the interesting thing is that these effects are not specific; each of these stimuli produces the same response, and since it has been recently shown that they are additive, in the sense that when two are applied simultaneously in subliminal concentrations so that neither would have an effect acting alone, the one reinforces the other and a response is produced. It would seem to follow that in this organism there is no specific response to light or any other sensory stimulus, but merely an indiscriminate reactivity of a general nature to them all. This curious one-dimensional world, this Flatland of sensation wherein the senses as we know them—for example vision and touch—are similar and additive, seems to me quite fascinating and intriguing.

From out of this primitive reactivity the various senses have become differentiated in evolutionary history. Alone, the thermal sense has shown no evolutionary off-shoots. From chemical stimulation has developed the fundamental sense of smell and its cousin, taste; from the response to mechanical agitation has developed the sense of touch and the vibratory sense with its extension to the sense of hearing; from photosensitivity has developed vision.

There may be other senses of which we have no conception. It could well be argued that termites or the blind driver ants of

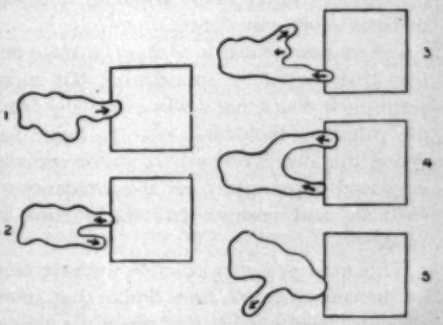

Fig. 2 (Duke-Elder). The behavior of the amoeba. The organism is moving onto the illuminated cover-glass of a microscope and eventually its movement is reversed (after S. O. Mast).

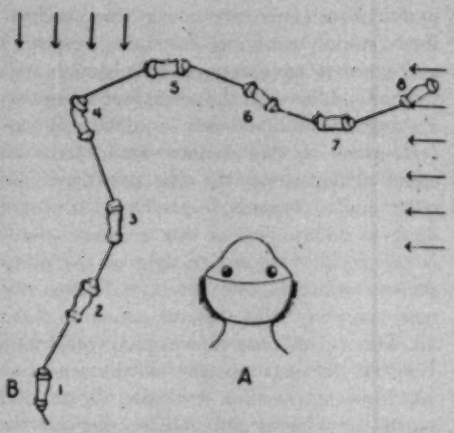

Fig. 3 (Duke-Elder). The response of the larva of Arenicola. (A) The head of the larva with two symmetric eyes. (B) The path of movement of the larva: in 1 to 4 the light is shining from above; in 5 to 8 it is placed at right angles (after S. O. Mast).

Africa must have some such faculty. They have no eyes; but the complexity of their social life in their teeming underground cities, not only as an ordered routine but with co-ordinated variations to meet unexpected emergencies of construction or war with equal facility, as well as the regimented discipline of their forays in the outside world, seem to demand some means of communication of which we know nothing, and perhaps can never know anything if it has no basis in our experience.

Let us now return to vision. To some extent that matter is speculative; but there seems little doubt that it was essentially from the primitive motor response to light that vision initially developed. It was eventually employed purposefully for the avoidance of obstacles and enemies and the pursuit of food.

This most primitive reaction we have seen in the amoeba. We find similar but more elaborate responses as we ascend the animal scale. Thus the green flagellate, Euglena, swims in a general sense away from a source of light; the finger-like larvae of the polychaete worm, Arenicola, toward it (fig. 3). In a further step forward the animal travels not directly toward or away from a light, but maintains a constant angle to it (fig. 4). This is an important advance wherein light does not act merely as a stimulus attracting or repelling the animal into a more favorable environment, but can be used as a means to an end, guiding it to a place where it wishes to go; the animal thus puts itself in the position of the pilot of a ship who can steer otherwise than directly in line with the sun or the pole-star.

Incidentally, in artificial circumstances this may have serious consequences. If the guiding light is sufficiently far away, as is the sun, the path of the insect is virtually a straight line; but if it is near at hand and the angle of incidence is to be kept constant, the insect must perforce fly along a logarithmic spiral ending in the light itself. It is for this reason that the moth, utilizing a mechanism designed for reference to the sun, flies to its death in a candle flame.

This directional taxis to light may reach astonishing accuracy. We shall take two examples of it as it is seen in insects and birds.

The compound eye of insects is ideally constructed for a function of this type. It is composed of a multitude of separate elements called ommatidia (fig. 5). As a ray of light passes from one to the other stimulating each at a time, the insect turns itself to maintain the constant stimulation of one element.

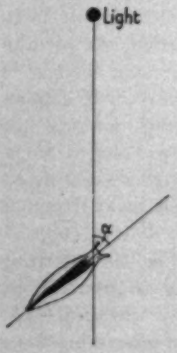

Fig. 4 (Duke-Elder). The orientation of a mollusc with respect to light. (α) is the orientation angle which the longitudinal axis of the mollusc makes with the direction of the light (after Fraenkel).

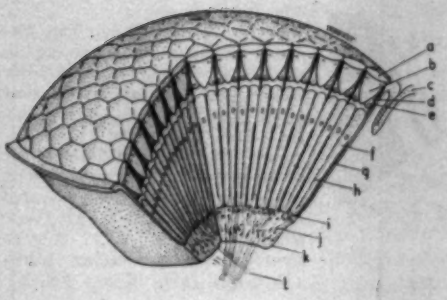

Fig. 5 (Duke-Elder). Diagram of a compound eye of an insect with a sector excised. (a) Corneal facet. (b) Crystalline cone. (c) Surface epithelium. (d) Matrix cells of cornea. (e) Iris pigment cell. (f) Cell of retinule. (g) Retinal pigment cell. (h) Rhabdome. (i) Fenestrated basement membrane. (j) Nerves from retinular cells. (k) Lamina ganglionaris. (l) Outer chiasm.

By blacking out different portions of the eye with varnish, it can be shown that the entire mechanism acts reflexly and automatically.

As an illustration, the behavior of the ant is interesting as it returns from far distances laden with food to its nest, a feat quite astonishing in an insect apparently lost in a forest of grass. The Swiss biologist, Santschi (1911), proved that it guided itself by the sun. If he shaded the insect from the direct light of the sun and reflected its rays from the opposite side by a mirror, the ant immediately reversed its direction. The German biologist, Brun (1914), went a step further. As the ant was going back to its nest, he imprisoned it in a box for two and one-half hours, during which time the sun had traversed an angle of 37 degrees in the sky; on being released the ant resumed its path still maintaining the same angle but now to the afternoon sun, and therefore travelling in a direction deviated by 37 degrees from its nest which, of course, it never reached (fig. 6).

von Frisch (1948-54), the delightful Austrian naturalist who has spent a long life in these studies, showed that bees are still more clever and do not make the same mistake. They appear to be possessed of an internal time-clock, as it were, in the brain, corresponding to the diurnal rhythms which occur in many animals and man. Not only can they, like the ant, orientate themselves with great accuracy by the sun, but they can, unlike the ant, make a correction according to the time of day. von Frisch, for example, accustomed a hive of bees to seek a feeding place 180 meters away in a direction 30°N of West during the afternoon (fig. 7). One morning he transported them to a hive in a different landscape and released them. The vast majority of the bees went to a feeding place 180 meters away, still in a direction 30°N of West, ignoring three other symmetrically placed sites. To retain the same orientation guided by the sun, the bees must have been able to calculate and allow for the solar movements with time, and the difference in the sun's direction in the afternoon and the morning. This is an extraordinary feat when it is remembered that the brain of a bee is only 1/10 of an inch in diameter; nevertheless, it is accomplished.

The navigational ability of birds is still more extraordinary; indeed, their capability

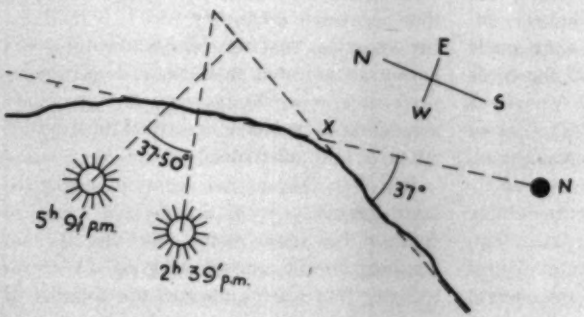

Fig. 6 (Duke-Elder). The orientation of the ant. The dark line indicates the route taken by the ant toward its nest (N). The initial part of its journey was orientated at an angle of about 90 degrees to the sun. At (X) the ant was imprisoned in a box for two and one-half hours, during which time the sun traversed an angle of 37.5 degrees. On its release the ant resumed its path, again at right angles to the sun, deviating from its former path by an angle of 37 degrees (after Brun).

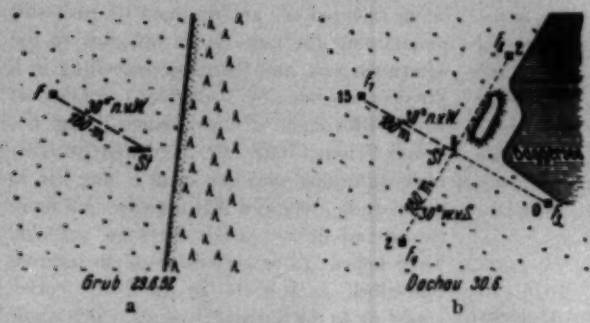

Fig. 7 (Duke-Elder). The displacement test in the orientation of the bee. In (a) marked bees from a hive (St) were allowed to feed in the afternoon from (F). In (b) they were transported to an unknown landscape and allowed out in the morning. Fifteen bees fed at a feeding place (F_1) 180 m. away in the direction 30°N of West. Relatively few (2, 0, 2) went to three alternative feeding places (F_2 to F_4) (after K. von Frisch).

of undertaking migrational flights from one continent to another to return to precisely the same locality has excited admiration and conjecture for centuries—from Africa, perhaps, to the same tree or the same loft in England. This apparently incredible faculty has recently been investigated by Matthews of Cambridge (1951-55). Among other experiments, he took the Manx shearwater to America and released it there. On an overcast day the birds flew indiscriminately in all directions, completely lost. On a sunny day, as they soared to fly, the birds orientated themselves correctly within 40 seconds, and homed 3,050 miles across the trackless Atlantic wastes to arrive after 12½ days, each in its own particular burrow on a small island off the west coast of England.

Consider for a moment what this means. The bird's eye is the most elaborate of any animal type, capable of resolution to 10 seconds of arc, that is, with some six times the accuracy of the eye of man. Matthews found that by keeping the birds in conditions wherein sun and light were excluded, constant errors in the flight home were made which could only be explained if the birds were failing to correct for the variations in the sun's altitude from which they derived their measure of latitude. By de-synchronizing the day-night rhythm before release by experimentally arranging an artificial day starting some hours earlier or later than usual, errors in longitude could be explained by postulating a disturbance of an inherent time-sense based on regular day-night sequences. The only explanation would seem to be that these birds can orientate themselves by estimating the sun's arc over a short distance and from this extrapolating its position at local noon, comparing this position with the remembered position at home, and making corrections according to a 24-hour rhythm maintain by a reference system (an internal clock) in the brain. All this certainly sounds fantastic particularly applied to a creature with a proverbially small brain; but the ability of a bird released in America to orientate itself so rapidly for a flight to a very precise locality in England is fantastic.

We have seen that the primary effect of light on the eye is the control of movement, and we have indicated the extraordinary lengths to which this potentiality may develop. We must now inquire to what extent are these motorial reactions automatic and reflex, and what part visual perceptions play in them. We know that the bird can see and that the bee can see, but in these reactions do they appreciate what they see? It is unlikely, for example, that the bird knowingly performs complicated mathematical extrapolations such as would appal most of us. Such a reaction as we have described must be instinctive and automatic.

But does the amoeba see as it moves toward or away from a light? We can go further, for these motor reactions are not confined to the animal kingdom. You remember that Carl Linnaeus, the botanist of

Uppsala, in his world-famous garden, still kept with reverent care by the Swedes, noticed the regular opening and closing of the flowers—the poppy which opened at 6.00 A.M., the speedwell at mid-morning, and so on. These you may say, are slow and static; but does speed matter? The Bengal plant Hedysarum girans, nods actively to a passing cloud. If we suppose that the clams see when they withdraw their siphons, or the snails their tentacles in the light, are we also to suppose that this applies to the plants which open their petals to the morning sun?

This is a question which is indeed difficult to answer. In the simple philosophy of Aristotle and for 2,000 years thereafter, no argument arose; plants had a vegetative soul responsible for growth and reproduction, to animals was added a sensitive soul governing movement and sensation, and to man a rational soul. But doubts began to occupy men's minds in the 17th and 18th centuries in the long disputation between the Cartesians who followed Descartes, and the mystic German nature-philosophers who talked of "vital force," the disciples of Paracelsus in the classical tradition, who found philosophic expression in Leibnitz and Goethe. To the first, the universe was essentially mechanical, driven automatically according to mathematical laws; to the second not only all living creatures but also minerals were permeated by a directive vital force. A middle view was expressed by Lamarck toward the end of the 18th century, who claimed that the lowest organisms were insensitive and that their conduct was governed by external driving forces derived from environment; but as the evolutionary scale was ascended, organisms generated their own appreciation to a progressively greater degree until vertebrates were reached at which stage intelligence became possible.

Each of these views has been maintained in recent times; the simple reflexology represented by Loeb and the Russian school of Pavlov on the one hand, and the purposive view represented by such philosophers as Whitehead, McDougall, and Russell on the other, a view wherein the vital force of the ancients has been replaced by the equally vague concept of the "general drive" or "action-energy" of modern biologists.

The mechanistic view would place the emergence of visual reflexes into the plane of consciousness as a late development. This attitude found its modern apostle in the person of Jacques Loeb. To him all the orientating and instinctive reactions of the lower animals to light or other stimuli were mechanically determined. Although it seemed to respond voluntarily and often purposively, the movements of a phototactic animal were those of a robot; it is forced to go where it is taken by its reflexly driven cilia, legs or wings, an activity in which consciousness or vision has no place. Even an ant, with all its proverbial intelligence, orientates its journey to light unthinkingly as does a sleep-walker or an automaton, and in this respect is as unteachable as a machine, completely totalitarian and incapable of individual adjustment.

It must be remembered that the new science of cybernetics has demonstrated that similar reactions, sometimes of astonishing complexity, can be carried out by nonvital mechanisms, those curious electromechanical first cousins of computing machines, which by a combination of photo-cells, amplifiers, motors, and automatic governing devices, can simulate many of the reactions of living things, not in appearance but in behavior, as they navigate themselves round the playroom of the electronic engineer. Figure 8 illustrates such a creation of Gray Walter of Bristol. Such mock-biologic robots, goal-seeking and self-regulatory, capable of the storage of information and possessed of a rudimentary type of memory maintained by electrical oscillations, have been constructed so that they can explore their environment with an apparent purpose. A photo-cell can serve as a receptor and amplifiers and motors can be interconnected in such a way that a positive taxis (for example) to a moderate

Fig. 8 (Duke-Elder). A cybernetic robot, avoiding a stool and making for the light (after Gray Walter).

light, and a negative taxis to a bright light (or to material obstacles or gradients, and other things) can endow it with the faculty to discriminate between effective and ineffective behavior, to seek actively an environment with moderate and optimal conditions, to acquire conditioned reflexes, and even to perpetuate its activity and "feed" itself with electricity by being optically attracted to a charging circuit when its batteries begin to fail. And if things go ill, just like an animal and more like a woman, it will work itself into a state of hysteria.

On the whole, however, it would seem that the matter is not so simple as this materialistic view would suggest. There is no doubt that to the higher animals vision is an act of perception, a mental as opposed to a reflex process, not merely an inevitable and automatic response but something which includes an element of appreciation and purpose and can be modified by experience. To decide when automatic reflexology became translated into perceptive appreciation, when mechanism first became interwoven with teleology, we must, I think, inquire when visual sensations can first be shown to modify conduct not in an automatic but in a purposive and intelligent way.

The most acceptable experimental procedure wherewith to analyze these reactions is a maze or discrimination box (fig. 9). The animal is allowed to go from the lower (outer) chamber into an inner compartment where two choices await him. At the far end of each are two visual stimuli, lights varying in intensity, perhaps, or color; with one is associated a reward (such as food), with the other punishment (such as an electric shock). The object of the exercise is to see whether the animal can be trained to dif-

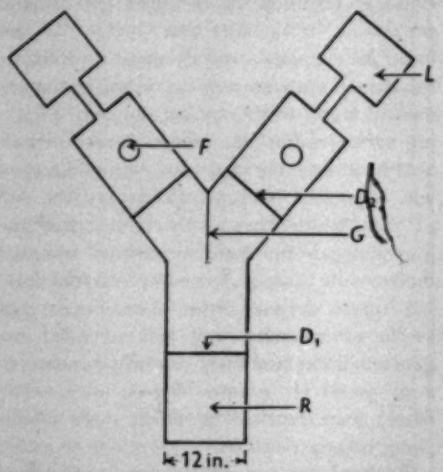

Fig. 9 (Duke-Elder). Discrimination box. (L) Light box. (F) Food. (D_1) Hinged door. (D_2) Hinged door with 3.0 by 3.0 in. opal glass panel. (G) Glass partition. (R) Restraining chamber (after R. Gunter).

ferentiate the one light-stimulus from the other while all other factors are kept constant. The method, of course, like all experimental techniques, has its limitations. The mere isolation of the stimulus, for example, is outside the animal's natural experience and forms an artificial enviroment, while the experiment may well break down if visual stimuli are not of importance in its life, so that they do not excite interest. Moreover, such experiments are limited to animals which are amenable to training, consistent in their behavior, and relatively intelligent and docile in their disposition, for it is impossible to train a stupid animal or one that gets cross or sulks.

In this way it has been shown, for example, that the cockroach, which normally avoids light, can be conditioned to go straight —and unnaturally—toward it, provided that it has been taught that a dark and comfortable shelter lies underneath it. Purposeful appreciation and experience can thus alter completely the automatism of the response, and indeed reverse it. It would seem impossible that an animal be trained visually to modify its conduct unless it can remember a previous visual experience, unless this experience had imprinted itself upon its consciousness, unless, in fact, the stimulus of light had given rise to a perception.

Where do such experiments take us? All investigations of whatever type so far undertaken have shown that in the three most primitive classes of animals—in protozoa, coelenterates such as jellyfish, and echinoderms such as the starfish—all responses to light are completely automatic and fixed. The first group in evolutionary progress to show some degree of visual intelligent appreciation is the worms. The earthworm has a great number of tiny simple eyes underneath the skin concentrated mainly at the head-end, and to some extent at the tail. In dim illumination it goes toward the light; in bright illumination it avoids the light. It follows that on emerging from its burrow at any time except at night or in the dim twilight of morning or evening, it will at once retract back into its burrow. Almost a century ago Darwin recognized that worms had a modicum of intelligence, for he noted the deft way in which by trial and error, profiting by previous experience, they transported suitable leaves of various types to their burrow or collected little stones to guard its entrance. We know that to the worm vision is relatively unimportant, for its life is dominated by its sense of touch and its exquisite sense of smell. Nevertheless, in a maze, propelled forward by a light from behind, and rewarded by food in a dark cell or punished by an electric shock, earthworms or aquatic worms can be trained to respond in different ways to light-stimuli and to acquire a complete reversal of their usual reactions.

The suggestion that worms are the first creatures to see may seem surprising; but, indeed, it is not. For we see, not with our eyes but with our brains, and the world we see is a symbolic representation of the outer world created by the central nervous system. Animals lower than worms have no centralization of their nervous systems. Some protozoa have conducting fibrils in their cellular structure to co-ordinate the movements of their cilia. Coelenterates such as the hydra have a complicated nerve-net. The starfish has a higher nervous organization with trunk pathways, but it also shows no centralization. All these animals show no intelligence or awareness in their reactions, no ability to profit by experience, no understanding to modify their conduct. For the first time in evolutionary history a centralized ganglionated nervous system appears in worms (fig. 10), and in them for the first time the responses to light are not entirely rigid and automatic, but are associated with motivation, incentive, and appreciation, are capable of modification by experience and training. Vision although still a secondary sense, for the first time becomes endowed with some degree of awareness and meaning: in short, the animal can see.

It is true that the amoeba may be imagined

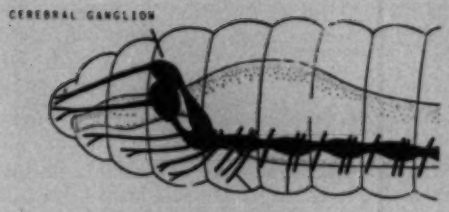

Fig. 10 (Duke-Elder). The ganglionated nervous system of an earthworm.

to experience some lowly kind of appreciation of light; it may be aware of the change in its environment and even associate the change with sufficient effective tone to allow it to be appreciated as something pleasant or unpleasant. But this is by no means necessary. We know of many reflexes far more complex within ourselves of which we are quite unconscious; and even if consciousness may be superimposed on them, it need not be necessarily or directly so. If some awareness does occur in the amoeba, we must logically surmise that this primitive sensation was part of a co-aesthesis in which the several senses as we know them are merged into one vague and indiscriminate unity in which stimuli—light, chemical, thermal, or tactile—which to us are distinct and unrelated, are co-equal and additive; but this is merely surmise, and for the surmise we have no basis in observed facts.

This is not to say, of course, that visual experiences at the lowliest level remotely resemble ours. The very simple eye of the worm cannot form an image of anything; all it can do is to appreciate differences in the intensity of light and perhaps the direction of its incidence. Its visual world can be merely one of light and shadow.

We have already seen that the primary response to light was the control of the animal's movement. There is little doubt that the next stage in visual evolution was the appreciation of movement in the outside world. This is a basic character, more primitive than the appreciation of form or color. Let us ascend the animal scale from worms and come to molluscs. The scallop has a multitude of brilliant emerald green eyes set like a diadem around its mantle. It makes no visual response to an object unless some movement is made; having seen it, it makes no attempt at visual analysis. Any movement of any object excites the same response—a protrusion of the tentacles which are provided with organs of the more fundamental chemical and tactile senses; these explore the object intelligently and on the results of their findings the animal either eats or flees. Likewise the snail, which has a simple eye perched at the tip of each posterior horn, appreciates light and movement. But vision is not of fundamental importance to it. In bright light or on stimulation, the eyes are retracted within the tentacles (fig. 11). Safety is ensured by the extreme tactile sensitivity of these animals to the slightest movement of the air or any jarring of the surface on which they crawl; while food is sought almost by scent alone.

Fig. 11 (Duke-Elder). The eye (E) of a snail retracted into the tentacle (preparation by Norman Ashton).

Even in the higher and more visually conscious animals, the appreciation of movement to a large extent dominates visual behavior, just as in the human eye the periphery of the retina, the most primitive and least organized part, is specifically adapted for this purpose. The fly takes no notice of the hand outstretched to squash it so long as the hand does not move; but on the slightest movement, the insect appreciates the danger and provokingly flies away. In the same way the rabbit will run into a stationary man, and a man is unseen to the wild animal as long as he remains motionless—and down-wind.

Form vision, or visual acuity, that is, the capacity to analyze and appreciate a pattern, is a later acquisition. The first proof we have of its existence is in the cephalopods, such as the octopus, creatures with eyes so well developed that they resemble those of man even although, as occurs in all invertebrates, they are entirely developed from the skin, not from the brain. In conditioning experiments wherein a particular figure was associated either with food or an electric shock, Boycott and Young (1950-56), of University College, showed that the octopus could be trained to differentiate between such formations as a cross, a square, or horizontal or vertical lines. The honey-bee can also be trained to feed from a sugar container placed beside a black disc and avoid one beside a black cross; but the ability of insects to analyze a pattern is poor.

Color vision is the last of the visual qualities to emerge, and it is of restricted incidence. Among invertebrates it has been proved to occur only in insects, which, indeed, have a more extensive spectrum than we, for they see far into the ultraviolet. Several types of insect have been trained to feed or to refuse food associated with different colors; and, indeed, the economy would seem to be biologically wrong that induced the entire vegetable world apart from the cryptogams to luxuriate in the riotous coloring of the flowers unless the insects which fed on their honey and incidentally pollinated them could appreciate their extravagance. Among vertebrates color vision occurs in some reptiles but has been shown to play an active part in behavior only in fishes, birds, and primates.

In tracing the development of the visual perceptions, as with all other functions, the most important determinant factor is found to be environment. To the animal which lives in the dark, vision is useless so that the eyes regress or even disappear. This applies to many of the inhabitants of the abyss of the oceans to which light does not penetrate, to fishes and amphibians which live in dark caves or burrow in mud, to creatures—termites and even mammals such as the mole—which burrow in the earth, and to internal parasites.

To animals which live upon the ground, vision has a biological value, but in the vast majority of cases it is a secondary sense. Most reptiles follow a trail, either of prey or their mate, by smell, the flickering tips of the tongue picking up odiferous particles from the ground and transferring them to Jacobson's organ in the mouth where they are both smelt and tasted. The blindfolded rattlesnake, for example, readily recognizes and viciously attacks its enemy the kingsnake; but, deprived of its tongue, an essential part of its olfactory mechanism, it lies passive even although it can see.

To most of the lower mammals, small creatures living close to the ground with a restricted horizon, often of nocturnal habits, vision is the fourth most important sense, the eye coming after the nose, the ears, and the tactile vibrissae. In their furtive lives, both food and safety are attained essentially by keeping their noses to the ground. It is true that as mammals grew larger and stronger, they felt able to roam abroad in the light of day, some relying for safety on their strength or ferocity, such as the carnivores, some on their fleetness, as the ungulates. In these, vision became more useful and the eye better; but the brain remained a nose-brain and dramatic progress was impossible. Vision

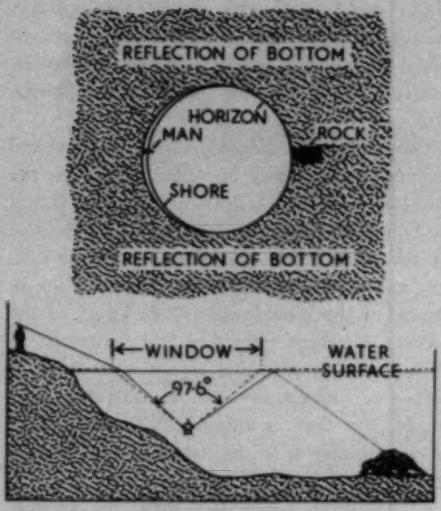

Fig. 12 (Duke-Elder). The upper visual field of a fish. In the lower figure the fish is seen swimming in fresh water and the paths of the rays of light are delineated. In the upper figure is shown the view seen by the fish with the central circular window of aerial vision near the periphery of which bodies become progressively foreshortened; around it is reflected a view of the bottom mirrored on the surface of the water (after G. Walls).

concerned itself essentially with moving stimuli, and visual analysis and color vision are absent.

The bull, for example, is color-blind, and the matador would excite the same wild response if, instead of his red cloak, he waved a piece of gray sacking so long as the bull sees something moving. Even the dog lives in a colorless world of gray monotones, its life dominated to a considerable extent by sounds which we cannot hear, for his hearing is 16 times more acute than ours, and scents of the acuity and diversity of which we have no conception; his feeding is regulated by smell and, deprived of his nose, even the urges of sex are lost. That is difficult for us to realize in our state of comparative noselessness.

For vision to come into its own the freedom and spatial scope of a tridimensional environment seems necessary. This to some extent is seen in fishes. As an example of the excellent visual judgments obtainable in fishes, the performance of the archer-fish, Toxotes jaculator, may be cited. It must be remembered that a fish is at a disadvantage when looking upward from water into the air. In these circumstances it must see through a window outside which, owing to the total internal reflection of light, the bed of the stream is mirrored; while within the window, because of the refraction of light at the water-air interface, objects out of the water become progressively foreshortened (fig. 12). Nevertheless, the archer-fish, while swimming, will spit a jet of water at an insect flying three feet above the surface with astonishing accuracy, overwhelming it in the air and devouring it when it has been brought down to the surface. This involves not only an excellent visual acuity but an equally excellent sense of direction, of judgment, and of distance (fig. 13).

Nevertheless, to the majority of fishes vision is a subsidiary sense, for most of them live happily and fully without vision although they normally use their eyes, their conduct being dominated by their chemoreceptors and the vibratory organs of the lateral line. It is to be remembered that in all

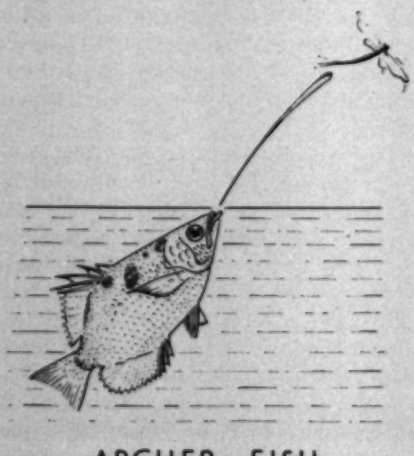

Fig. 13 (Duke-Elder). The archer-fish shooting a jet of water at a dragonfly flying above the water.

cases water is not a good medium for accurate vision, and in the abyss darkness is absolute. In the high lakes of the Alps, the fish are as well and prosperous-looking after the seven or eight months when the water is covered with a layer of ice and snow sufficiently thick as to preclude all light, as they do in the sunlit water during the short months of summer. Blind cave-fishes are as alert and well-fed as their sighted cousins, and in the aquarium artificially blinded rays or skates acquire their food and conduct themselves in a way indistinguishable from normal fish.

For the full development of vision animals had to get above the ground. In the air the adventure afforded by the third dimension, the necessity of distant exploration and the absence of other sensory stimuli such as smell or touch, all served this purpose. For this reason among invertebrates, insects have the highest visual powers and alone have a fully developed color sense. Similarly among vertebrates birds attain the highest visual acuity and again have color vision. The reactions of fear by the shrike which the falconer carried with him in a cage let him know the whereabouts of his bird-of-prey long after he himself had lost track of it in the sky; and the African vulture will spot dead game lying on the ground, to us completely camouflaged by its surroundings—and recognizes that it is dead—from a height of 4,000 meters, a height so great that a man cannot discern the bird in the sky with its three-meter wing-span.

Even among reptiles the arboreal types which get above the ground have excellent vision. In contrast to its cousin the ground snake, the tree snake has remarkable eyes, set forward to attain binocular vision, each provided with a fovea; it hunts with its eyes, not with its tongue. Among this class of animals the stimulus to vision of life in the trees is nowhere better seen than in lizards: the chameleon, for example, hunts for insects by vision. It is a sluggish animal, but its two eyes, standing out as it were on turrets, swivel around quite independently of each other looking for insects. As soon as one is seen in the vicinity, both eyes converge forward upon it, and with incredible rapidity and unfailing accuracy, the long sticky tongue shoots out as far as the length of its body to capture its prey, a feat requiring excellent visual judgments.

But in all these classes a cerebral cortex is unavailable for visual appreciation so that their optical powers, excellent although they may be, are not fully realized. The cerebral ganglion of the insect is essentially dominated by rigid reflex reactions; and in the brain of the bird visual appreciation is relegated to the tectum in the midbrain, and, although its optical imagery is the most perfect we know, a perceptual symbolism is lacking to match it (fig. 14). Only in mammals does vision find cortical representation, and only when they left the prison-house of the ground did vision come into its own. This tendency is seen even in the family of squirrels, lowly rodents far down the scale in the mammalian class, which have excellent eyes.

First in the tree-tops of the tropical rain forests every stimulus was presented in every variety, and most of all visual stimuli. The first creature to have a brain potentially capable of evolving into an eye-brain was our remote ancestor, the tree-shrew. The interplay of the tropical sun on the foliage, the

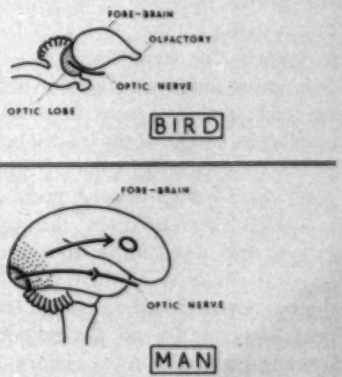

Fig. 14 (Duke-Elder). Visual pathways and brain.

Fig. 15 (Duke-Elder). The red-eared monkey. (Zoological Society of London.)

flowers, the fruit, the insects, and the birds, stimulated the development of the color sense, which appeared first among mammals in the capuchin monkeys; and in these it is interesting that it appeared as a two-color system as occurs in protanopic color blindness in man. The environment of the tree-tops allowed our ancestors to throw away the shackles of the sense of smell, all-important for survival upon the earth beneath them. In this swaying habitat, springing from branch to branch, fine stereoscopic vision and perfect spatial judgements became necessary for survival; to miss your foothold—or your handhold—meant, at the least, a broken limb; so that in place of being merely used for running, the forelegs became prehensile hands accurately correlated in the cortex with vision; thus was laid the foundation for the physical dexterity of man. The security of the tree-tops allowed an escape from the urgent fears of life on the ground, with its teeming population of predators, so that the senses, not constantly alert for danger, turned to other things. Together the eyes and the hands explored new objects, giving rise to new associations within the brain, the birth of curiosity and inventiveness; thus was laid the foundation for the intellectual supremacy of man (fig. 15).

When the first tree-shrew left the ground in fear for the safety of the trees, it was indeed a poor thing; but it had inadvertently chosen an ideal evolutionary forcing-house; and when the ape-man descended from his cradle in the trees with an eye-brain in place of a nose-brain, freeing his hands by becoming bipedal, safe in his new intelligence and cunning, he became the lord of the earth. He reached the critical point at which physical dexterity could combine with conceptual thought and the faculty of speech, and thus a new method of evolution became possible based on the transmission of cultural experience rather than on the transmission of physical qualities alone. He had become modern man.

It is important to realize that in the animal kingdom generally, the parvenu sense of vision is not particularly associated with effective tone as other more fundamental senses seem to be. Its function is to register, and its role passive. The peahen doubtless views with interest the color display of the peacock's tail; but the interest is probably an instinctive sex-association, and not a vivid aesthetic emotion. No dog gazes with rapture at the glories of a sunset or a rainbow in the same way as the cat revels in the warmth of a fire or purrs to the tactile luxury of stroking. To many lower mammals, scents may have an urgent meaning, sometimes of danger, perhaps sometimes of ecstasy; but vision, no.

Apart from instinctive responses, the only species to show visual curiosity and appreciation, an interest in exploring the potentialities of vision in an experimental fashion, are the higher anthropoid apes. The chimpanzee, for example, will amuse himself by looking at the world in different ways—by looking upside down, by bending down and looking

through his legs, by punching a hole in a leaf and pearing through it, or by making a pool of urine and regarding his reflection therein. This is the beginning of something new and big. It is the first indication that vision has become elevated from the level of biologic usefulness to approach that of aestheticism. To the lower animals a visual perception seems to be merely the appreciation of something that repetitive experience has taught them to presage good or ill for their lives, their stomachs, or the perpetuation of their species. Now in the chimpanzee, and presumably in his cousin, the ape-man, we see the emergence of a new quality, of an active rather than a passive character, a quality by virtue of which we, his descendants, look at a sunset or a rainbow and call it beauty.

Here then is how I picture the emergence of vision in the animal world—stated in terms of Lloyd Morgan's theory of emergent evolution or Wundt's creative syntheses. As complexity in evolution increases, every now and then a stage is reached when something new and surprising emerges, something which could not have been foretold because it represents something greater than the summation of its constituent parts. When atoms come together they form a molecule with properties quite unlike the atoms. When the appropriate molecules combine in bewildering complexity, life is formed; at a later stage—or perhaps contemporaneously—consciousness emerges. In a philosophy such as this I see the development of vision in the animal world in three emergent stages.

We start with a *motor taxis*. This first appeared when life began in the simplest unicellular organisms, as a reaction initially automatic and rigid, not necessarily associated with consciousness. It eventually became more plastic when visual perceptions became available to react with it, and it reached its culmination in the homing capacities of birds.

The second emergent I would call *perceptual vision*. It deals with practical things in a pragmatic way, the eye a photographic camera dealing first in light alone, then in movement, then in form, and eventually in color too, and the brain a receiving screen, but acting essentially as a passive register. It emerges when a brain-ganglion appears in worms, for it needs a central nervous organization to weave its symbolism on the receiving screen. At first it takes a minor and eventually a major part in the determination of conduct, concerning itself primarily with the biologically urgent instincts of hunger, fear, and sex; and its function is merely to observe and to report.

The third emergent I would call *imaginative vision*, endowed with artistic and creative qualities, charged with an inquisitive, exploratory drive. Its emergence waited on the almost explosive development of the forebrain and the association areas in the highest primates. It first appeared, presumably, during the ape-man's arboreal adventure, and certainly its early beginnings are seen in the chimpanzee, and it was well established when modern man migrated northward from Africa following the melting of the ice, 20,000 years ago, to draw the pictures of the Aurignacian and Magdalenian civilizations in the caves of Southern France and Northern Spain; it reaches its greatest development, perhaps, in the human mind relieved of the chemical servitude of inhibitions, as by mescalin, under the influence of which visual appreciation becomes charged with an exquisite poignancy.

Granted, then, that animals including worms and above this level, see, the question arises, what do they see? Granted that they see the same world around them that we do, full of the same things with the same kaleidoscopic variations in relationships, what do they make of it all? We do not know. The territory-holding male robin pays no attention to an exact stuffed replica of itself so long as the breast is brown; but will attack viciously a formless untidy mass of feathers, so long as they are red. Even in man, an analysis of perception is impossible. The brain of each of us creates a symbolic repre-

sentation of the outside world, but this personally created world of symbols is our own and private. How sure are we that we all see the same blues, and yellows, and reds; and have we tried to visualize the world as it appears to the color-blind? To some the painting of Picasso is more full of meaning than is the *Mona Lisa*, just as to some the glory of an opera of Wagner is but a noise.

And if in our wordy thinking we find difficulty in submitting our own perceptions to scientific analysis, how much more insecure are we when we try to analyze the experiences of the dumb creature? As we reason by analogy and experiment within the different groups of animals, we are sure of one thing with certainty—that each species has its own perceptual world, and that each of this multitude of worlds bears little or no resemblance to the environment of the animal as we interpret it in terms of our own private perceptual world.

It must be remembered that a perceptual pattern arises from many different sensory impressions which present no additive qualities among themselves, some derived from the outside world, others from the individual himself. The impulses from the outside world are integrated in the central nervous system, be it a simple ganglion or a ten-thousand-million-celled brain. This is brought about by the facilitation of the accustomed and the inhibition of antagonistic impressions, a process in which a thousand are inhibited to allow the passage of one, for only by the exclusion of the irrelevant can the important hold the stage. These are interwoven on a basis of inherited dispositions and past experience to form a perception. The conditioning influence of experience is continuously changing and essentially plastic in its nature. The inherited dispositions vary profoundly between species and even between individuals within a species. The final product is thus individualistic and capricious; it lies outside the physical laws by which we are accustomed to formulate the conduct of material events; it carries with it the suggestion of a new creation rather than an ordered sequence of cause and effect, a computed product of in-put and out-put; and, to complicate it all, like a melody it is four-dimensional, for it exists in time as well as space.

This, of course, is not to say that there need be anything supernatural about the process; it is merely to say that it cannot be explained by the physico-chemistry that we have at our disposal, nor is it susceptible to such mathematical formulation as we know today or are likely to know tomorrow. Indeed, so far are we from understanding that if we argue that our own perceptual symbolism is the only real thing and the outer world is nonexistent, none can gainsay us.

And, if I may surmise, I think it unlikely, as Parsons (1927) put it, that such a tomorrow will ever come within the experience of any of us for lack of adequate measuring-rods. Even if we analyze our own perceptions, knowledge of physical things can only be made available to us through our senses. A table cannot know of a chair; we must ascend higher to the level of physiology and look down to measure and weigh them with our eyes and our fingers. Sensations can only be appreciated and interpreted by our perceptions. Vision knows nothing of hearing; we must ascend higher to the level of psychology and again look down for such analysis. Similarly to explore perceptions we must perforce climb another stairway and again look down at the level beneath. Such a stairway may indeed exist, but with our limited mental endowments we cannot see it, far less climb it. In the storey above there may exist a God who can look down, or there may be nothing—or even a psychiatrist. But that is not science; it is belief—or agnosticism—or self-deception.

It may be that some day we shall be able to climb to such heights. We have seen what the brain of a bee can do within the limits of $\frac{1}{10}$ inch in diameter; who can say that the brain of man with its 1,400 cubic centimeters has reached the limits of its potential

complexity. That the neurosurgeon can remove large parts of it without apparent disadvantage would seem to indicate that it has not. During the last 10,000,000 years of our arboreal and postarboreal life, the brain of the ape-man has expanded three-fold in volume. Who can say that its progress is now frozen? Who knows what hydrocephaliclike monstrosities our descendants of 10 million years hence will be? The step between ape and angel may not be so big as we think. New capacities and understandings may emerge; but that is not today; we cannot yet look beyond vision to the Void, and through the Void at objective reality; and, of course, in assessing the potentialities of human progress in the next 10 million years, or indeed of human survival, we must remember the snag that the apes threw sticks and stones while we throw atom bombs.

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PHOTOCOAGULATION OF THE RETINA*

Report of a successfully treated case of angiomatosis retinae

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The first reports on the utilization of visible light in the experimental production of chorioretinal burns were given at the 17th International Congress of Ophthalmology in 1954 by Meyer-Schwickerath of Germany.[1] At this same congress, Byrnes, Brown, Cibis, and Rose[2] reported their retinal burn experiments in rabbits exposed to the fireball of atomic explosions in Nevada. Earlier this same year we had become interested in retinal burns as related to atomic explosions and a laboratory research program for elucidating some of these problems for the Air Force was implemented. These experiments, carried out by the Department of Ophthalmology in close collaboration with the Department of Biophysics, have recently been concluded. From these experiments it became apparent that controlled retinal burns, as suggested by Meyer-Schwickerath, can have clinical application. In this paper we report the clinical employment of our experimental technique in the treatment of a macular lesion.

In our retinal burn studies, we employed a 24-inch carbon arc searchlight equipped with an ellipsoidal mirror and modified for use with 10-mm. Hitex positive and Orotip negative carbons. These carbons operate at 140 amperes, giving a current density of 190 amp/cm.[2] The spectrum is roughly equivalent to a black body at 5,800°K., but

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is peaked in the visible range and deficient in the infrared range. A second ellipsoidal mirror is employed to reduce the angle of convergence from 28 to about seven degrees. The angle of convergence of light upon the cornea is adjustable by means of a limiting aperture placed 42 inches in front of the cornea. The retinal image diameter is a function of the angle of convergence. Irradiance at the cornea ranges from 1.3 to 1.5 cal/cm.^{2}/sec. for the maximum cone of radiation (seven degrees). Maximum irradiance available at the rabbit retina is approximately 70 cal./cm.^{2}/sec.

The threshold dose for minimal lesions on the rabbit retina was determined for various rates of delivery, image sizes, and pulse shapes. Severe lesions were also produced and studied clinically and histologically. The results of these experiments have been described in detail in a previous report.[3, 4]

After evaluating our results completely, we felt justified in trying our experimental set-up clinically, although it was primarily designed as a research tool. Realizing that our present set-up was too cumbersome for coagulating lesions in the retinal periphery, we were forced to await a fortuitous central retinal lesion, which finally presented itself in May, 1957, in the person of a 30-year-old white man who stated that the day before he awakened with a dark circle in front of his right eye. No history of injury or previous involvement of his eyes was noted. His general health was good. Family history was negative. Examination revealed both eyes to be externally normal. The visual acuity in the right eye was 20/400 and the left eye, 20/20.

The right fundus showed in the central area a large, somewhat reddish, elevated pigmented mass which had a few flame-shaped hemorrhages over the temporal surface associated with some small, hard, white exudates (fig. 1). This large vascular tumor was fed by a dilated and tortuous artery and drained by a vein of similar character. Several other dilated vessels could be seen

Fig. 1 (Guerry, et al.). Appearance of angioma before treatment.

on the surface of this tumor. The left eye was normal in every respect. A diagnosis of a von Hipple angioma of the right central area was made. Neurologic examination was entirely negative. The visual fields showed a dense central scotoma of 10 to 20 degrees in the right eye (fig. 2).

Twelve days after we first saw the patient, a light coagulation of the angioma with

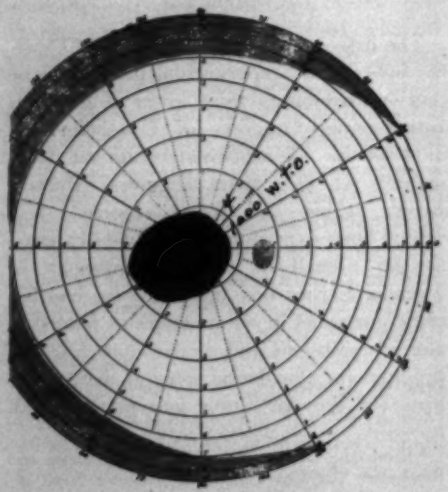

Fig. 2 (Guerry, et al.). Central scotoma before treatment.

the apparatus previously described was carried out. Three exposures of 322 msecs. each, utilizing a 4.5-inch aperture which produced lesions of about 1.2 mm. on the retina, were placed straddling the tumor. The retinal irradiance for each of these exposures was 23 cal/cm.²/sec, giving a retinal dose of 7.3 cal./cm.² The central portion was not directly hit. After the second exposure, small retinal hemorrhages appeared and a slight vitreous haze was noted. The exposures were easily seen as white, round, coagulated areas about one disc diameter in size. The next day, the patient had some pericorneal injection and epiphora which was attributable to ultraviolet rays. This cleared readily under local steroid treatment. Several days later, the vitreous had cleared completely and the burns were visible and confluent. The vessels were smaller, but the angioma itself was unchanged.

One week after the first exposure, two exposures of 500 msecs. each, with the same set-up, were given, the only change in technique being the insertion of a 0-52 filter into the beam to filter out ultraviolet radiation. The retinal irradiance for each of these two exposures was 18 cal./cm.²/sec. mounting to a retinal dose of nine cal./cm.² These two exposures caught the vascular tumor in its center, also just above and just below, the feeder vessel being directly hit where it entered the tumor. Several retinal hemorrhages appeared again, and a slight vitreous haze was noted.

After several days, the angioma had noticeably shrunk, the principal feeder artery being markedly constricted and sheathed, and most of the other large vessels had disappeared. A tremendous amount of whitish material was scattered around the lesion, particularly below, representing lipoid material such as that noted after destruction of similar lesions treated by diathermy (fig. 3). One month later a considerable amount of that whitish material had disappeared.

At the end of four months a small, discrete white scar could be seen in the area of the tumor, the feeder vessel being almost completely obliterated by sheathing. Some retinal striae radiated toward the periphery (fig. 4). These appeared as a result of scar shrinkage. Seven months after the first treatment the fundus is unchanged except that the striate reaction is much less pronounced and the lipoid material deposits have almost disappeared. No retinal detachment has occurred. The vision five months postopera-

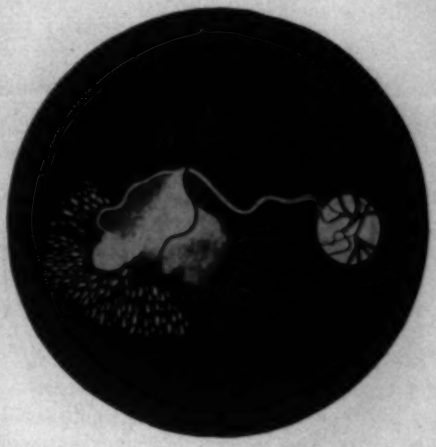

Fig. 3 (Guerry, et al.). Appearance of tumor one week after second series of coagulations.

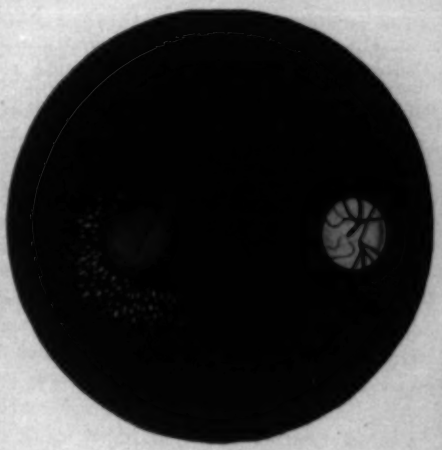

Fig. 4 (Guerry, et al.). Appearance of lesion seven months after treatment.

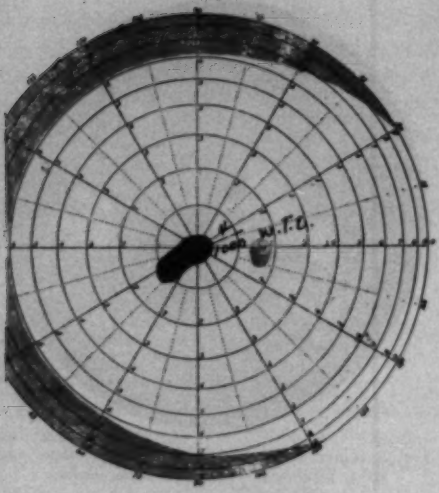

Fig. 5 (Guerry, et al.). Central scotoma seven months after treatment.

tively was 20/400 in this eye and at eight months has improved to 20/100. Visual fields show a dense central scotoma, approximately one third the size of the preoperative scotoma (fig. 5).

While no hard and fast conclusions can be drawn from one case, we feel it safe to say in agreement with Meyer-Schwickerath that photocoagulation of the retina should have a place in the treatment of retinal lesions. Tumors, flat detachments, Eales' disease, perhaps acute chorioretinitis and lesions of such ilk, lend themselves naturally to such therapy. With the development of a less cumbersome apparatus, this form of therapy should open up new therapeutic vistas.

Summary

A case of a von Hippel angioma of the central fundus has been successfully treated with a carbon arc light source originally developed for retinal burn studies in the rabbit eye.

2015 Monument Avenue (20).

We wish to express our appreciation to F. Schmidt, R. C. Williams, R. S. Ruffin, and M. C. Shaffer for their technical assistance and constructive criticism.

Addendum

Since this paper was written, we have utilized a Zeiss light coagulator in a number of animal experiments and three human cases of retinal detachment. The irradiance at the cornea available with this apparatus is about 40-percent greater than the irradiance in our experimental set-up when measured with the waterflow calorimeter. In addition, this machine provides a surprising versatility and ease of operation which makes it noticeably superior for clinical use. We are more than pleased with its performance.

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OCULAR TOXOPLASMOSIS*

The XIV Jackson Memorial Lecture

Michael J. Hogan, M.D.
San Francisco, California

It is an unusual honor to be invited to present this lecture in memory of Dr. Edward Jackson. Fortunately I knew him for a few years before he died. Even at his advanced age it was obvious that he was a man of great simplicity and good humor, and that he possessed an active and inquiring mind. He was constant in attending meetings, and we encountered Dr. Jackson frequently at meetings on the Pacific Coast. At that time my wife worked in her father's [H. G. Merrill, M.D.] office. At these meetings he delighted in discussing basic problems and perplexing her with unusual refractive and muscle problems.

I asked some of Dr. Jackson's associates for reminiscences about his days in Denver and at various meetings. Many of them dealt with his ability as a teacher, his devotion to ophthalmology, and the manner in which he made Denver a mecca for ophthalmologists. Apparently he was unostentatious, dressing and practicing in a very simple manner. His office was not ornate, and I was informed that it was common for him to make house calls on a bicycle or in a model T Ford.

One of the best tributes came from one of his former pupils, Dr. Phillips Thygeson, and I have asked permission to quote him verbatim:

"It was wonderful knowing Dr. Jackson. He was not only one of the ablest but one of the gentlest and kindest men that has ever graced our profession. I wish I had the words to put over a little of his flavor and charm and essential goodness."

Introduction

Human toxoplasmosis is one of the most interesting diseases of modern medicine. Its manifestations are protean and, in the acquired form, resemble those of a number of well-known disease entities. At first glance it is surprising that diagnostic studies have failed to show the frequency of this disease. However, one of the important diagnostic tests, the methylene blue dye test, is technically difficult and involves the risk of handling live organisms. These factors probably have restricted widespread testing and have prevented more rapid progress in the diagnosis of the disease. The evolution of our knowledge of this disease has followed the pattern usually observed in infectious diseases; it was first discovered in various animals and birds, and many years later in humans. The eye manifestations of this disease are important and have been subjected to considerable study. It is important at the present time that the entire subject be reviewed, and that additional information be presented with regard to ocular involvement.

In 1908 Nicolle and Manceaux[25] reported the finding of organisms similar to Leishmania in a North African rodent, the Gondi. They found the organisms to be widespread in the tissues, but, unlike Leishmania, the kinetoplast was absent. In the following year these authors gave the organism the name Toxoplasma.

Since publication of these reports, spontaneous Toxoplasma infections have been observed and reported in a wide variety of

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I wish to express my thanks and appreciation to Miss Ann Lewis and Mrs. Phyllis A. Zweigart for their assistance in conducting these studies and in preparation of this paper.

wild and domestic animals and birds, including those used for experiments in laboratories. In a number of instances different names were assigned to the strains isolated from various species, but studies soon verified the fact that all were members of the same species. All strains appear to be serologically and biologically identical but differ considerably in their virulence.

It was not until 1938, however, that Wolf and his co-workers[43] discovered toxoplasmosis in man. They reported the isolation of Toxoplasma from a 31-day-old infant who developed an acute and fatal illness within a few days of birth. Clinically this infant suffered severe encephalomyelitis and bilateral chorioretinitis. These findings were verified at autopsy. Toxoplasma organisms were observed in microscopic sections and isolated from experimental animals which were inoculated with the infant's tissues. This study also was the first to show that an apparently healthy mother could give birth to an infected infant.

Following the study of Wolf and his coworkers, many reports of congenital toxoplasmosis were published. Most of these reports indicated that lesions of the eye, the central nervous system, and the viscera were common.

Although congenital toxoplasmosis has been considered in the past to be a rare disease, there now is evidence that many infants are born with unrecognized infections. The congenital nature of the infection may be discovered only in those cases where a later flare-up occurs.

It was suspected by many for a number of years that some forms of chorioretinitis in older children and adults might be due to acquired types of toxoplasmosis, but methods to prove this were lacking until the discovery of the toxoplasmin skin test in 1947[13] and the methylene blue dye test in 1948.[33] The dye test is based on the principle that antibodies in the patient's serum are able to prevent live Toxoplasma from staining with methylene blue (table 1). A substance in fresh normal human serum, probably properdin plus complement fraction, known as accessory factor, is necessary to accomplish this reaction. The highest dilution of serum in which over 50 percent of Toxoplasma are unstained is the end-point.

By using the skin test in population surveys it was demonstrated that there was an extremely high incidence of toxoplasmic infections throughout the world. Feldman and Sabin[12] first showed that the incidence of positive skin tests rose from five percent in persons in the age group from five through nine years to 50 percent in those in the age group from 30 through 40 years, and to 65 percent in those over 40. With minor variations other observers confirmed this finding in the United States and European countries. Subsequent studies with the dye test supported these findings.

It is my intention to review some of the important advances in our knowledge of toxoplasmosis, the epidemiology of the disease, its diagnosis, and treatment. Emphasis will be placed on the results of our studies in

TABLE 1

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Antigen (Organisms from mouse peritoneal fluid)	+	Antibody (Patient's serum)	+	Accessory Factor (Fresh normal human serum)

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the diagnosis and treatment of the ocular form of this infection.

Biology of Toxoplasma

Toxoplasma is classified as a protozoan parasite. It is an obligate intracellular organism which reproduces by longitudinal fission within a host cell or in its vicinity. It measures four by seven microns and is crescentic in shape in its extracellular form. Within cells and after fixation it is somewhat rounded. Prolonged survival in tissues leads to formation of pseudocyst forms in which numbers of organisms are surrounded by a capsule which stains with silver.

Toxoplasma does not withstand drying, freezing, and ordinary chemical action. In Tyrode's solution or in mouse peritoneal fluid it can survive up to four weeks at ordinary refrigeration temperature. It can be grown in animals, eggs, or tissue culture. A wide variety of cells can be used to maintain the organisms in tissue culture, although the yield of organisms is usually low.[20]

Toxoplasma is pathogenic for a large number of mammals and birds. It can be propagated by direct transfer of infected tissues or fluids into healthy animals, cell cultures, or fertile eggs. Infection of animals can be achieved by inoculation of organisms by any route. A parasitemia follows growth at the site of inoculation and persists for a variable period, depending on the host, the virulence of the Toxoplasma strain, and the numbers introduced. Antibody formation results and can be detected at a suitable interval after the inoculation. The organisms spread throughout the body but seem to prefer the tissues of the central nervous system, where they may persist for years. This persistence also occurs in the eye, for we have demonstrated that organisms can be recovered from the chorioretinal tissues up to two years after inoculation into the vitreous of the eyes of guinea pigs.[19]

Epidemiology

Skin tests, and serologic and cultural studies in man, birds, and animals (wild and domestic), have shown that toxoplasmosis is frequent and widespread. Sporadic cases and epidemics have been reported from practically all portions of the world. Feldman and Miller[11] studied 10 human and 24 animal populations with the methylene blue dye test. There was a low incidence of positive tests in Eskimos, Navajo Indians, and Icelanders. In various urban populations in the United States, 17 to 35 percent of the sera were positive at titers of 1:16 or above. A higher incidence of positive tests at 1:16 or over was found in Haiti (36 percent), Honduras (64 percent), and Tahiti (68 percent). They found that 27 percent of laboratory guinea pigs and five percent of rabbits had antibodies. Laboratory rat and monkey sera were negative. Serum titers varied in dairy herds from completely negative in two herds to 48 percent in another (all in the same locality). Groups of dogs, sheep, and swine showed variation of serum dye test antibodies. These and other studies indicate the wide prevalence of the disease.

The method of spread of this infection in individuals and species is incompletely understood.

It is known from animal epidemics[2] that large numbers may die and that Toxoplasma is found widely distributed throughout their tissues. In isolated cases Toxoplasma has been found in the urine of infected rabbits and dogs and in feces from dogs with a type of hemorrhagic colitis. It has been demonstrated in muscle tissue, heart, liver, and spleen of many diseased animals.

Experiments prove that healthy mice can be infected by ingestion of other mice recently dead of an infection[24] and that infected mother mice can transmit the disease to the nursing offspring of healthy mothers.[4] Weinman and Chandler[29] transmitted the

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disease by feeding pigs and rats the tissues of other pigs, rats, and mice infected with a Toxoplasma strain isolated from pork. Van Thiel and van der Waaij[37] showed that consumption of tissue containing Toxoplasma pseudocysts leads to infection in mice and guinea pigs.

The site of entry of the organisms in causing human infections is not known. The foregoing studies suggest that oral transmission may be important. However, it is most likely that the disease is transmitted by various means. The results of investigations on transmission by arthropods and insects are inconclusive, and further study is indicated.

Clinical manifestations

Human toxoplasmosis may appear in various forms, which often resemble other diseases and are not diagnosed as toxoplasmosis because they are not recognized as such.

The following modified classification of toxoplasmic infections as outlined by Frenkel[14] and Siim[36] is acceptable and will be discussed as listed.

I. Congenital
   A. Apparent
   B. Inapparent
II. Acquired
   A. Exanthematous
   B. Meningoencephalitic
   C. Lymphadenopathic
   D. Ocular

I. Congenital toxoplasmosis

Early reports on congenital toxoplasmosis gave the findings in infants born with manifest infections, or who developed such infections within a short time after birth. Most infants had severe lesions of the central nervous system and the viscera. Mental retardation, hydrocephalus, and other sequelae were common.

It now is apparent that the disease also exists in a milder form and subsides without obvious sequelae.

Apparent infections

The stage of pregnancy at which infection takes place, the virulence of the organism, and fetal or maternal resistance determine the type of infection in the newborn infant. The disease is transmitted to the fetus from a mother who acquired the infection during pregnancy, and the organisms most likely reach the fetus through the placenta.[10] The method of acquisition of the maternal infection is unknown, but all such infections occur without symptoms. Mothers who have given birth to toxoplasmic infants do not infect subsequent offspring. This suggests that maternal immunity is important in preventing acute toxoplasmosis in the fetus. It is not proved, however, that nonapparent infections do not occur in the fetus during subsequent pregnancies. Infection with organisms of low virulence also may result in milder infections, as illustrated in the subsequent report of one of our cases.

Infection early in pregnancy results in fetal death. Infections in midpregnancy cause widespread disease in the fetus, resulting either in death with miscarriage, or causing such severe damage that the infant is born with marked sequelae of this disease (hydrocephalus, microphthalmos, and so forth). Infections occurring late in pregnancy are associated with the acute manifestations of toxoplasmosis. Encephalomyelitis (generalized convulsions, fever, various paralyses), chorioretinitis, and visceral involvement may be observed. The infant may or may not survive. At other times the acute manifestations do not appear until a few days after birth. Eichenwald[5] found that 30 percent of his patients with congenital toxoplasmosis were probably infected late in intrauterine life, because they were born with an acute generalized febrile disease and variously exhibited jaundice, anemia, diarrhea, vomiting, lethargy, and irritability. Examination of these patients revealed an enlarged liver and spleen, petechias, and purpuric or small erythematous papules with necrotic

centers. An interesting observation was that six infants had a low-grade fever and irritability, without other manifestations, and recovered completely without developing chorioretinitis; however, two of them later showed mental retardation.

Inapparent infections

Some infants are born with the disease, which is unrecognized by the physician or parents. At a later date the child may exhibit serologic or clinical evidence of the infection. Some cases which have been reported as examples of acquired toxoplasmosis in children may, in fact, be examples of an activated phase of a congenitally acquired infection. In our experience this has been especially true with respect to ocular disease.

Chorioretinal inflammations

A. Acute

1. Present at birth or shortly thereafter and associated with acute systemic disease
2. Developing after birth, and not always associated with acute systemic infection

B. Subacute

C. Late relapse of a healed chorioretinitis

Acute chorioretinitis, present at birth or shortly thereafter, is one of the most constant lesions to occur in congenital toxoplasmosis. It is most often bilateral and may occur in multiple foci. The disc and peripapillary region are commonly affected. Lesions occurring in this area most often lead to serious visual loss. The fundus lesions are usually found in those children with systemic manifestations of toxoplasmosis. In 1953 Feldman[8] studied 103 cases in which the diagnosis was based on the clinical and serologic findings. He found chorioretinitis in 99 percent, and it was bilateral in 85 percent.

Eichenwald[5] found 40 percent of 75 toxoplasmic infants to have chorioretinitis at the first examination. The frequency increased to 80 percent when the survivors were examined subsequently. He later presented the results obtained in a series of 140 patients, of which 80 percent showed evidence of chorioretinitis.[6] Six of the 28 patients who did not show chorioretinitis at birth developed eye lesions within two weeks to six months after birth. Four of these six patients eventually showed bilateral involvement.

This later appearance of the chorioretinal lesions is fascinating and indicates a possible intermittent parasitemia. The infection in such patients may smoulder, with intermittent relapses, parasitemia, and involvement of other organs. Verlinde and Makstenieks[38] repeatedly isolated Toxoplasma from the cerebrospinal fluid and blood of four living infants having hydrocephalus, calcification of the brain, microphthalmia, and chorioretinitis (one case as long as two months after establishment of the diagnosis). Relapses of congenital ocular toxoplasmic infections, often with lesions in new areas of the fundus, suggest that infections may spread from rupture of pseudocysts and dissemination of organisms by the ocular fluids.

Pathology. The acute chorioretinal inflammation commences in the retina, with copious exudation into the vitreous, producing a marked haze (fig. 1). The foci are poorly

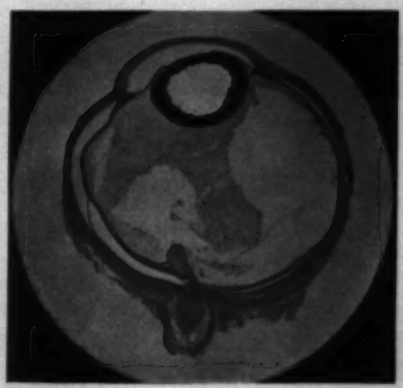

Fig. 1 (Hogan). Congenital toxoplasmosis, acute chorioretinitis.

Fig. 2 (Hogan). Congenital toxoplasmosis, acute chorioretinitis, and papillitis.

defined and usually quite large (figs. 2 and 3). Secondary involvement of the choroid causes marked elevation (fig. 4). Small satellite foci are common. The acute phase of the inflammation lasts from two to four months, depending on its severity and the presence or absence of new foci. Organisms can be found in cysts or free in the acute lesions (fig. 5). After healing, the lesions are atrophic and pale with a variable amount of pigmentation at the margins (figs. 6 and 7). Pseudocysts may be found in the tissues adjacent to healed lesions. These are parasitized cells containing resting, viable organisms and are surrounded by a membrane which stains with silver. Rupture of these cysts may lead to reactivation of the disease.

Diagnosis. One cannot make a definitive diagnosis based on the clinical appearance of the eye lesions. It can be made with some certainty when combined with the associated systemic findings and by the serologic studies. The normal infant may have a low titer of dye test antibodies in his serum which persists up to four or five months after birth, as the result of passive transfer from the mother. The toxoplasmic infant is born with a high titer of antibodies if the infection developed early in the mother's pregnancy, or it develops increasing amounts of antibodies if the infection developed nearer term. The dye test antibodies develop within three to four weeks after onset of the disease and rapidly reach a high titer, whereas complement fixing antibodies do not develop until five to six weeks after onset of the infection. Both types of antibodies persist in fairly high titer for five to six years, then gradually decrease. Any dye test titer in a child below age 10 is of great significance, because surveys have shown that normal children below this age rarely show any antibodies against toxoplasmosis. A combination of acute disease of the eyes, the central nervous system and the viscera, with a high or rising dye test antibody titer, usually establishes the diagnosis. Animal inoculations of blood and spinal fluid from suspected cases should always be made, if possible, for a definitive diagnosis.

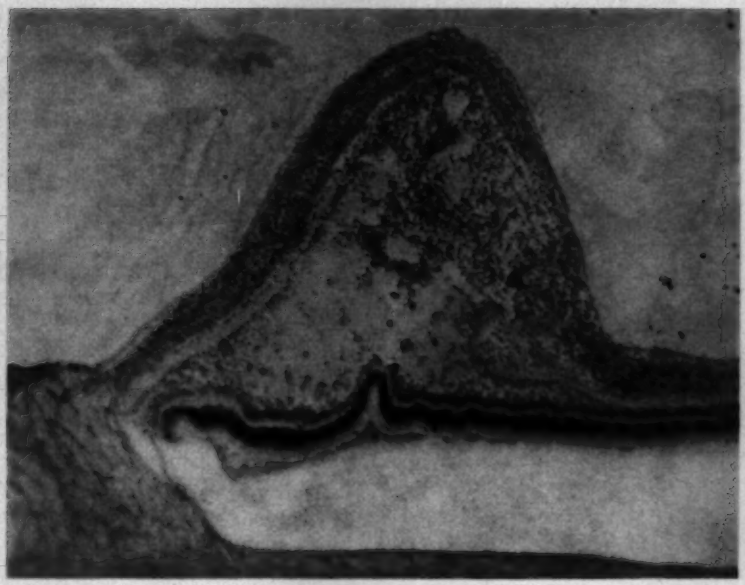

Fig. 3 (Hogan). Congenital toxoplasmosis, focal retinitis.

Subacute chorioretinitis may develop in a toxoplasmic infant who shows no signs of systemic disease, or who has had such mild signs that they are unrecognized. Such infants later may show evidence of damage to the central nervous system and may develop recurrent convulsions or other neurologic disorders. Examination of the eyes shows chorioretinal lesions which may be active or almost completely healed. The diagnosis in this group can be made with the same certainty as in the acute group.

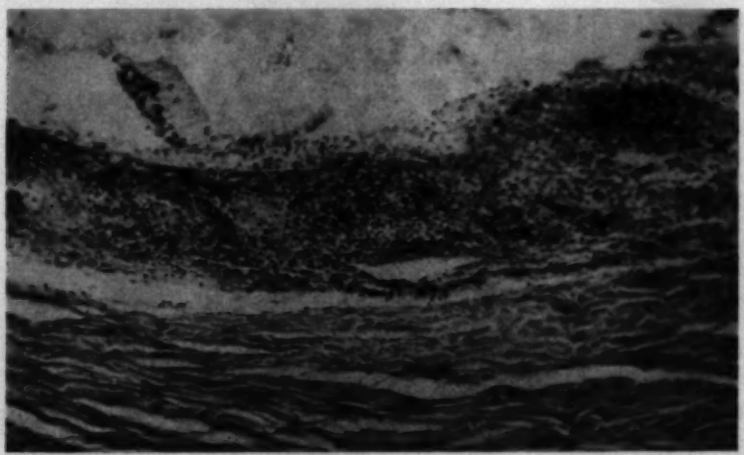

Fig. 4 (Hogan). Congenital toxoplasmosis, acute choroiditis with necrosis.

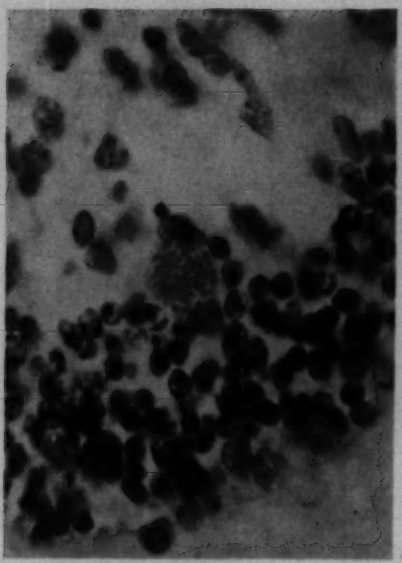

Fig. 5 (Hogan). Congenital toxoplasmosis, intracellular Toxoplasma in retina.

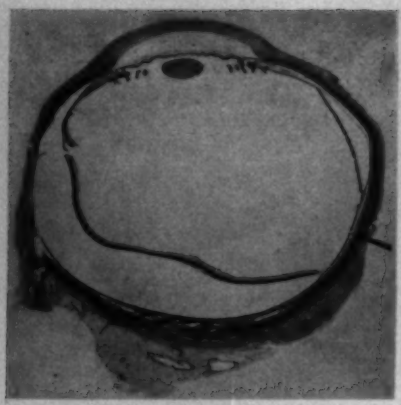

Fig. 7 (Hogan). Chorioretinal scar, congenital toxoplasmosis.

Acute or subacute chorioretinitis in children beyond the stage of infancy becomes apparent to the ophthalmologist in a variety of ways:

1. The child develops an esotropia or an

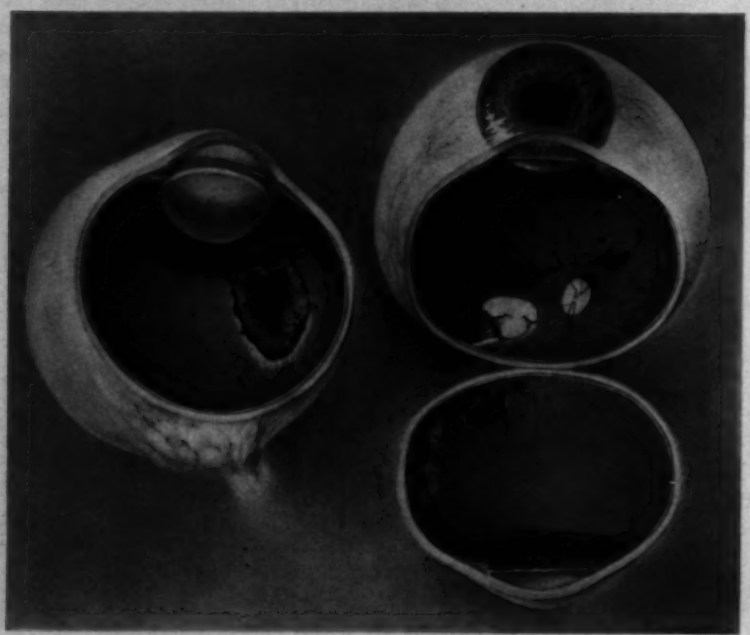

Fig. 6 (Hogan). Healed foci of chorioretinitis in congenital toxoplasmosis.

TABLE 2

FINDINGS IN 36 CASES OF CONGENITAL TOXOPLASMOSIS

Type		Onset			Late Relapse	Strabismus	Dye Test			Skin Test				Skull X-ray			
Uni-	Bi-	0–6 Mo.	6–12 Mo.	12 Mo.			<1:128	1:128–1:512	>1:512	+	−	±	Not Done	+	−	±	Not Done
11	25	8	9	19	12	20	14	13	9	22	9	1	4	7	21	7	1

exotropia. This results from macular or paramacular scarring, which can be observed easily on fundus examination. Roentgenograms of the skull may or may not show calcifications, and the blood usually reacts positively to dye and complement fixation tests. The child may show no evidence of cerebral damage or mental retardation, and he may be in perfect health otherwise.

2. The child is discovered to have reduced vision at the time he commences school, when the nurse checks the visual acuity. Examination shows changes in the fundi similar to those described previously, and general studies are substantially the same.

3. A *late relapse* of the chorioretinal inflammation occurs, causing progressive visual deterioration. Examination shows a chorioretinal scar with an adjacent new focus of chorioretinitis. This late relapse of congenital ocular toxoplasmosis has not been emphasized sufficiently. The only previous references to this aspect of the disease are those of Woods and his colleagues[44] and of Eichenwald.[6] It should be repeated that many toxoplasmic infections are so mild that they are not recognized. In other infants the signs exhibited during a particular illness may not suggest the diagnosis of toxoplasmosis. The ophthalmologist and the pediatrician often are surprised to find an older child having clinical and serologic evidence of toxoplasmosis without a history of any previous acute illness.

Studies on congenital toxoplasmosis

In a routine survey of over 1,500 patients with various forms of endogenous uveitis, we encountered and have previously reported 28 patients with probable congenital toxoplasmic infections involving the eye.[17] Some of these were accompanied by evidence of systemic disease, while others were not. We have studied eight additional cases, making a total of 36 (table 2). In addition to these, we have found four interesting examples of a late exacerbation of congenital toxoplasmic chorioretinitis.

The mothers of all 36 children had normal pregnancies, and there was nothing in the history which would suggest a maternal toxoplasmic infection. Some had the usual contacts with household pets. An occasional mother had contact with domestic farm animals, but a history of illness of any of these animals was not obtained. Thirty-four of the infants seemed normal at birth except that one had feeding difficulties and another had signs suggesting cerebral palsy.

Strabismus (esotropia or exotropia) was the first and most common eye complaint, being present in 20 of the 36 children. It most often resulted from amblyopia due to macular inflammation or scarring. In 25 children the chorioretinal lesions were observed in both eyes, usually in the macula of one eye and at some other site in the other eye. Multiple foci were common. Only one patient showed a microphthalmia. The ocular disease became apparent to the parents of eight patients before the sixth month after birth, and in nine other patients it had a very early onset. Roentgenograms of the skull revealed no abnormality in 21 children, and showed positive signs of toxoplasmosis in seven children. No roentgenograms were made in one case and in seven cases the interpretation of the roentgenogram was questionable.

Twenty-two patients had positive skin

tests, nine were negative, one was questionable, four were not tested. Nine patients had negative skin tests, but did show positive dye tests, often in high titer. This would seem to demonstrate that the skin test alone cannot be used for the diagnosis of congenital toxoplasmosis.

Fifteen children 10 years of age or below had positive dye tests as follows: Six were 1:512 or greater; six were 1:128 to 1:512; three were below 1:128. The dye test titers in the 36 patients were as follows:

Titer	Number of Patients
1:16	5
1:64	9
1:128	3
1:256	8
1:512	2
1:1,024	3
1:4,096	1
1:8,192	2
1:32,768	2
+ neutralization test	1
Total	36

It is interesting that 12 of these 36 patients had late childhood or adult relapses of chorioretinal inflammation. In some the fundi showed old chorioretinal scars with newer acute inflammatory areas in a "satellite" position.

Case report

Late relapse of congenital toxoplasmosis. Two of these cases have been reported but will be recorded again in brief form to demonstrate the nature of this type of case.

Case 1*

M. F., age 12 years, a white boy, was first seen because he had sudden diminution of vision in his good left eye. At the age of one and one-half years he was found to have a chorioretinal scar in the macula of the right eye. There were no further difficulties up to the age of 12. Examination showed the right vision to be 15/200 and the left to be 20/200. The right macula contained a large area of healed chorioretinitis (fig. 8). A heavy vitreous haze was evident in the left eye, and an indistinct

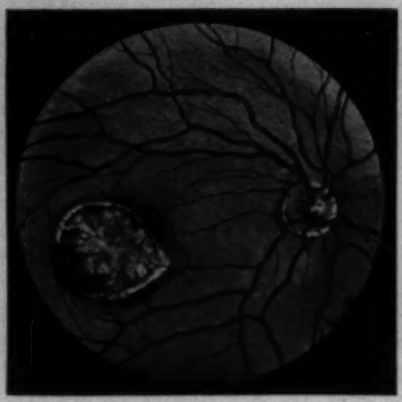

Fig. 8 (Hogan). Case 1, right eye, congenital toxoplasmosis.

massive yellowish area of inflammation extended from the disc to the temporal periphery (fig. 9). Roentgenograms of the skull showed calcifications (figs. 10 and 11). The methylene blue dye test was 1:128, and results of both the skin test and the neutralization test were positive.

Course: The course of the disease is shown in the accompanying table (table 3). Five months after the onset of the disease the left vitreous had cleared so that vision was 20/70. Two and one-half years later the lesion was fairly well healed and vision was 20/100.

There was extensive scarring and pigmentation of the entire temporal fundus, particularly along the horizontal meridian. Relapses occurred in this eye, and vision was eventually lost. The eye became divergent, hypotonic, and cataractous, and commenced to shrink. Enucleation was requested and

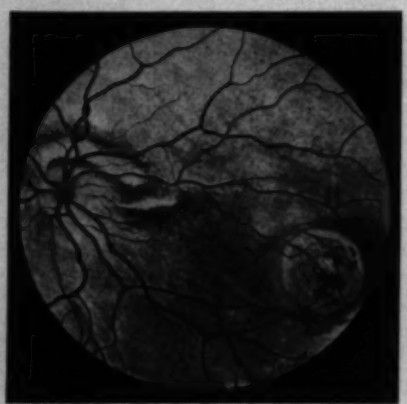

Fig. 9 (Hogan). Case 1, left eye, congenital toxoplasmosis.

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Fig. 10 (Hogan). Case 1, cerebral calcifications, congenital toxoplasmosis.

accomplished in 1956. The eye was opened under sterile conditions and showed extensive scarring of the retina (fig. 12). The scarred area was used for cultures, only a small amount being saved for histologic study. Toxoplasma was isolated in mice from the healed lesions in this eye. The organism recovered has been found to possess a low virulence for mice, requiring from eight to 10 days to produce illness instead of the usual four required by the more virulent RH strain. When a small inoculum is made, the mice become ill but recover and live indefinitely, although most show some sequelae of the encephalitis. Inoculation results in significantly positive dye test titers in mice, and in previously

Fig. 11 (Hogan). Case 1, cerebral calcifications, congenital toxoplasmosis.

negative rabbits and guinea pigs after inoculation by various routes.

Comment: This is a most interesting case in that it demonstrates a probable persistence of the organisms in the eye for 20 years following a typical congenital infection.

CASE 2

M. W., aged 11 years, a white boy, was first seen at the age of 11 years because of blurred vision in both eyes. Information was obtained that reduced vision had been discovered in the right eye at the age of 10. A general examination for a cause of this condition was negative. The patient was referred to me with the possibility that the eye lesions were of toxoplasmic origin. It was reported by letter that a methylene blue dye test in November, 1954, at the Communicable Disease Center, Chamblee, Georgia, showed a titer of 1:64. There had been no systemic infection between the ages of 10 and 11 years.

At our first examination in December, 1955, the eye lesions were completely quiet and fundus examination showed bilateral healed macular scars, more

TABLE 3

HISTORY AND FINDINGS IN A CASE OF CONGENITAL TOXOPLASMOSIS

Case 1: Patient M.F.

Age	1½ years	12 years	20 years
C-R	RE, macular, healed	LE, acute, temporal, diffuse	LE, secondary glaucoma
Dye test		1:128	
Skin test		Positive	
Laboratory		X-ray+	Toxoplasma isolated from enucleated LE

Fig. 12 (Hogan). Case 1, chorioretinal scarring in congenital toxoplasmosis. Toxoplasma recovered from this eye on inoculation into mice.

marked in the right eye (fig. 13). Vision in the right eye was 16/200 and in the left, 20/30. The methylene blue dye test titer was 1:4,096. Roentgenograms of the skull were negative, and the results of the skin test were negative. Results of an examination in May, 1956 were essentially the same, and the dye test titer remained at 1:4,096. A relapse of the inflammation in the left eye occurred in March, 1957, without causing a change in dye test titer but causing reduction of vision to 20/80. The patient was treated with Daraprim and sulfadiazine and Meticorten by mouth, and the response seemed good. By May, 1957, vision was improved to 20/50 and the lesion was healed. The dye test at this time was 1:256.

Comment: This type of early recurrence is the typical form observed in most of our cases of congenital toxoplasmosis. One might argue that this

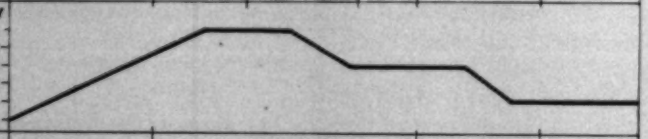
DATE	11-54	12-55	5-56	8-56	3-57	5-57
VISION	AGE 10, BLURRING BOTH EYES	R.E. 16/200 L.E. 20/30	R.E. 16/200 L.E. 20/30	SAME	R.E. 16/200 L.E. 20/80	R.E. 16/200 L.E. 20/50
FUNDI	BILATERAL HEALED MACULAR SCARS OBSERVED		HEALED SCARS, BOTH MACULAS	SAME	RELAPSE IN L. MACULA	HEALED
SEROLOGY 1:4,096 1:2,048 1:1,024 1:512 1:256 1:64						
SKIN TEST	NEGATIVE					
SKULL X-RAYS	NEGATIVE					
THERAPY					DARAPRIM SULFADIAZENE	

Fig. 13 (Hogan). Case 2, history and findings. Congenital toxoplasmosis with a late relapse.

TABLE 4

TOXOPLASMIC CHORIORETINITIS
PATIENT A.L., AGE 36 YEARS, FEMALE

1936	1943	Feb.–May 1955
Acute chorioretinitis, LE studies negative	Acute chorioretinitis, LE	Acute serous pleurisy
	Central vision loss	Diagnosed and treated as tubercular
	Pyrotherapy	
Cleared in 6 mo. after T & A	Cleared in 3 wk. leaving macular scar	No acid fast organisms demonstrated
← R.E. CLEAR →		

patient acquired his toxoplasmic infection at the age of 10, but we feel that it is of congenital origin because of our observance of undoubted congenital cases of identical type.

CASE 3*

A. L., aged 36 years, a white woman, was referred for examination because of blurred vision in her good right eye. She had a choroiditis in the left eye at age 15, and a recurrence at the age of 22. The last attack left markedly blurred vision in this eye (table 4).

Early in 1955, while on Okinawa, she developed pleurisy, dyspnea, headache, and fever. One week later a pleural effusion was discovered. The patient was returned to the United States and was treated with streptomycin and Isoniazid for six months for possible tuberculosis. In August, 1956, six months after finishing the treatment, blurred vision developed in the right eye, although the patient thought it might have commenced in the latter part of 1955. A rather large area of peripheral choroiditis was found in the right eye and vision was 20/20. The left eye showed a large macular scar (fig. 14), although vision was 3/200. Skull plates were negative. The accompanying graph (fig. 15) shows the results of serologic studies and treatment.

Comment: This patient could have developed an acute pulmonic (acquired) toxoplasmosis in 1955, with subsequent spread to the right eye in 1956. We think it more likely that the chorioretinitis at ages 15 and 22 was due to congenital toxoplasmosis, and that the probable pulmonic relapse was due to rupture of a pseudocyst.

We feel that some of the cases diagnosed as acquired toxoplasmosis are, in fact, late relapses of congenital infections. Several of the cases we have studied which have had such relapses have developed high dye test titers, suggesting that the relapse somehow reawakens antibody formation. Sabin[31] stated that his observations led him to believe that high amounts of toxoplasmosis antibody may result from subclinical reactivation of the latent infection. He described a patient who suffered a recurrence of a toxoplasmic infection, probably as the result of pseudocyst rupture, and were it not for some routine serologic studies which were being carried out, this relapse would not have been detected by those observing the patient.

Differential diagnosis

The systemic manifestations of congenital toxoplasmosis must be differentiated from other infectious and degenerative diseases of the central nervous system. The ocular lesions are not diagnostic in themselves, but when coupled with the other signs they are suggestive. If the child shows only the ocular changes, one must depend on the result of

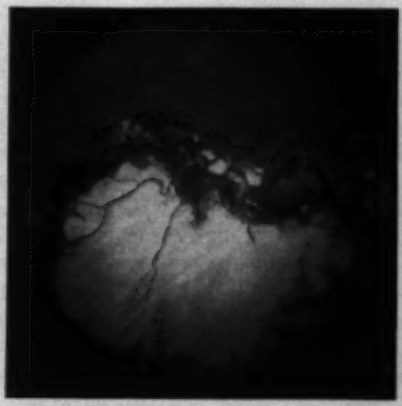


Fig. 14 (Hogan). Case 3, macular scar, left eye, due to chorioretinitis at the age of 15 and 22 years.

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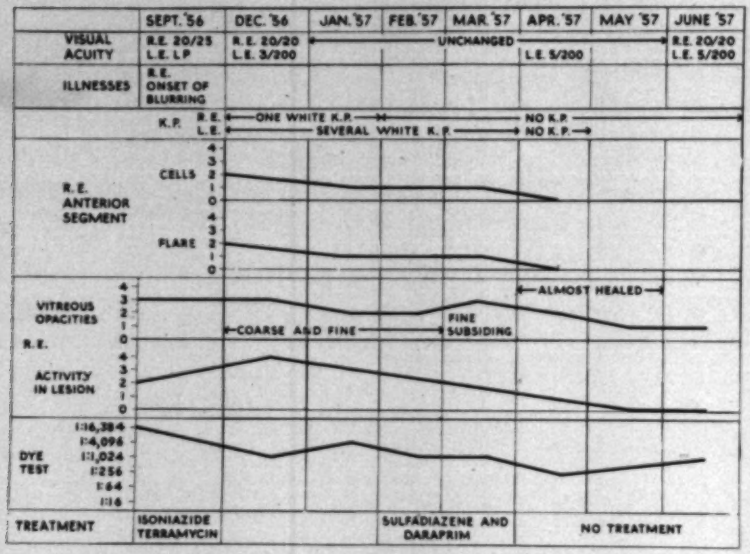

Fig. 15 (Hogan). Case 3, congenital toxoplasmosis.

serologic studies. One of the conditions to be differentiated was first reported by Sabin and Feldman[35] and discussed in detail before this society in 1949. In this syndrome the infants exhibit all the manifestations of congenital toxoplasmosis, yet they do not have positive serologic tests nor can Toxoplasma be isolated from the tissues. This disease has come to be known in pediatric circles as the Sabin-Feldman syndrome. The recent report of Weller and co-workers[40] of the isolation of an intranuclear inclusion producing virus from urine and liver aspirations of infants with illnesses resembling cytomegalic inclusion disease fits in with this entire picture. The latter infants had chorioretinal lesions and disease of the central nervous system similar to that reported by Sabin and Feldman. Christensen and his colleagues[1] also reported a case in which such lesions were observed in the brain, and at autopsy cytomegalic inclusion virus was demonstrated in the eye and brain tissues.

Other congenital inflammations of the eyes resulting from the spread of infection from the mother to the fetus must be differentiated from toxoplasmic disease. The absence of positive results on dye tests rules out toxoplasmosis.

II. Acquired toxoplasmosis

A. Exanthematous

A number of cases of the exanthematous form of acquired toxoplasmosis have been reported. The disease resembles a rickettsial infection with a sudden onset, chills, fever, and development of a maculopapular eruption during the first week. The widespread involvement is suggested by the development of pleuritis, a dry cough, myocarditis, and encephalomyelitic symptoms. Most cases have been fatal. Eye involvement has not been recorded.

B. Meningoencephalitic

The meningoencephalitic form appears to be rare, the first case being reported by Sabin.[30] This six-year-old boy had a fever, became unconscious, had generalized convulsions, and developed lymphadenopathy. Ex-

amination showed a large number of mononuclear cells in his spinal fluid. At autopsy Toxoplasma was isolated from the brain, and there was a diffuse meningoencephalitis. Other cases have been reported by Siim (Denmark),[36] Feldman (United States),[9] and Giroud and co-workers (three cases from North Africa).[16] These patients had illnesses similar to that reported by Sabin. The patient whose case was reported by Feldman also had an exanthematous skin reaction. Eye involvement has not been observed.

C. Lymphadenopathic

The lymphadenopathic form will be reported in more detail because it may be the type which eventually causes eye lesions. Siim[35] in 1950 described such cases in a group of children. This investigator and others have emphasized the frequency with which this form occurs compared to other types. The three recognized forms are (1) a febrile lymphadenitis. (2) a nonfebrile lymphadenitis, and (3) a subclinical form.

Febrile lymphadenitis may have an acute or gradual onset with chills and fever, general malaise, headache, and localized or generalized lymphadenitis. It resembles infectious mononucleosis except for the negative results of the heterophile antibody test. The fever and lymphadenitis gradually subside over a period of three or four weeks. One case reported by Siim had retinal exudates and very fine hemorrhages in one eye. It is possible that this was due to febrile retinopathy. Results of the methylene blue dye and complement fixation tests become strongly positive late in the disease. Siim was able to isolate Toxoplasma from affected lymph nodes in a number of cases.

The *nonfebrile* form may be discovered by the patient or the parent. It may be evidenced by enlarged lymph nodes in an otherwise healthy patient.

The *subclinical* form apparently is uncommon. Siim reported the case of a healthy girl who was admitted to the hospital for study of an oligophrenia of nine-years duration. A routine dye test showed a high titer, and examination then revealed some enlarged axillary and inguinal nodes. A node was excised, and Toxoplasma was isolated from it upon animal inoculation. According to Siim, results of clinical examination of these patients with lymphadenitis were normal except for enlarged nodes, which are of hazelnut to walnut size, relatively nontender and generalized.

In the group of lymphadenopathy patients the disease runs a benign course, with complete recovery within a few weeks or months, but with the nodes often remaining enlarged for a year or longer. Lassitude was a common accompaniment of the convalescent period. It is interesting that only one of about 100 cases showed a chorioretinitis. The dye and complement fixation test became positive in one month, reaching dye test titers of 1:1,000 to 1:10,000 and complement fixation titers of 1:50 to 1:100. A relative lymphocytosis of 50 to 70 percent was present in the blood.

According to Siim,[36] the histologic picture in the nodes is so characteristic that it should suggest the diagnosis and warrant serologic studies. Examination of sections of excised lymph nodes shows hyperplasia of the reticulum cells and islands of large eosinophilic cells scattered over the whole of the section.

To confirm the diagnosis, the surgically removed lymph nodes were minced, and the heavy tissue suspension was injected intraperitoneally into mice. An inapparent infection resulted, and at the time the mice were killed six to eight weeks later the results of the serologic dye tests were positive and Toxoplasma organisms were recovered from the tissues. Siim reported the isolation of Toxoplasma in this manner from the lymph nodes of 10 patients. Subsequently, Desmonts and Le Tan Vinh[3] isolated Toxoplasma from the nodes of seven out of 19 subjects suspected of having acquired toxoplasmosis and exhibiting positive dye test

titers. In 27 control patients it was not possible to isolate organisms from nodes.

D. Ocular

Early studies indicated that some cases of adult chorioretinitis were due to toxoplasmosis. It was soon learned that chorioretinal inflammations are rare in acute acquired systemic toxoplasmosis in contrast to their incidence in congenital toxoplasmosis. The reason for this is uncertain but it has been suggested that fetal retina is more susceptible to such infections. The occurrence of toxoplasmic chorioretinal inflammation in the absence of obvious systemic disease would seem to nullify this concept.

The ophthalmologic literature, however, contains a number of reports of ocular toxoplasmic infections, many of which are based on insufficient evidence. The probable diagnosis of ocular toxoplasmosis cannot be made solely on serologic evidence unless there is an unusually high titer, or at least a fourfold change in titer in paired sera. Even such changes as this must be regarded conservatively. One should beware of making positive statements based solely on the serologic findings.

A conclusive diagnosis of a toxoplasmic infection can be made only by isolation of Toxoplasma from the fluids or tissues of patients with acute illnesses. Such a requirement is impossible in those patients with ocular toxoplasmosis because these patients rarely have associated systemic infections and uncommonly show changes in serum dye test titers. Most often the ophthalmologist must be content with very presumptive laboratory and clinical evidence.

Frenkel[15] observed that those patients with positive results on skin tests had an earlier onset of chorioretinitis than those with negative results, and that the incidence of positive results of skin tests in patients with chorioretinitis far exceeded the incidence of positive results in a control group.

Wising[42] reported the first case of acquired ocular toxoplasmosis occurring during the course of a systemic disease. The infection occurred in the later stages of a febrile illness in a 31-year-old woman with a generalized lymphadenopathy. The serum of this patient showed a marked rise in dye test titer during the course of the illness, and the complement fixation test showed the characteristic delayed rise in titer. A number of other reports followed in which the presence of acute chorioretinitis was associated with a high or rising antibody titer.[18, 24, 27, 28, 44]

Following this, surveys on patients with chorioretinitis showed a higher incidence of positive results from dye and skin tests than in a similar group of the "normal" population, suggesting that a number of cases are toxoplasmic. The difficulty is that most patients with chorioretinitis who have positive results on tests also have very low titers. A number of investigators have tried to establish the significance of various dye test titer levels. Our group feels that any patient with chorioretinitis who has a positive titer at 1:16 or higher should be suspected of having ocular toxoplasmosis, provided that no other cause can be established. A single positive result does not prove that the patient has ocular toxoplasmosis; it serves only as a guide to indicate the possible presence of the disease.

The incident needed to stimulate further work was provided in 1952 by the studies of Wilder[41] in a report showing that organisms with the morphologic characteristics of Toxoplasma were present in the necrotic retina of chorioretinal lesions in 53 human eyes. These lesions were quite characteristic in that the principal focus seemed to lie in the retina, with secondary granulomatous reaction in the choroid and frequent thickening and inflammation of the overlying sclera. The disease was unilateral in most cases. The disease in most of these eyes had been considered on clinical or pathologic grounds to be ocular tuberculosis. Jacobs, Cook, and Wilder[21] obtained 21 samples of sera from this group of patients at a later date. The

following titers were found: one undiluted; one at 1:2; one at 1:4; seven at a titer of 1:16; four at 1:32; four at 1:64; two at 1:256; one at 1:2,048. There was some immediate objection to a morphologic diagnosis of ocular toxoplasmosis on these reported cases but, as one observer remarked, "What else could they be?"

In 1956 Jacobs and associates[23] analyzed the results of the skin test and the methylene blue dye test performed on 193 adult patients with uveitis. Eighty-six of these patients had a nongranulomatous form of the disease and 107 had a granulomatous type. The diagnostic criteria employed for the diagnosis of ocular toxoplasmosis in an individual case were as follows:

1. An ocular picture believed compatible with Toxoplasma infection.

2. A positive toxoplasmin skin test, with the dye test positive to a minimum titer of 1:64.

3. Exclusion of other systemic granulomatous infections.

With these criteria, about 35 percent of the 106 cases of granulomatous choroiditis were attributed to toxoplasmosis. This research team found an 80 percent correlation between the skin test and the dye test in this group. In this and a former series, a total of 79 cases of ocular disease were found which could be considered to be toxoplasmosis. Fifty-one of the patients showed a focal choroiditis or chorioretinitis; seven patients had old granulomatous chorioretinal foci with secondary acute allergic reactions superimposed; 17 had generalized uveitis; and four had retinal periphlebitis.

The final proof that Toxoplasma can cause chorioretinitis in adults was furnished by Jacobs, Fair, and Bickerton[22] in 1954. They isolated Toxoplasma from the infected eye tissues of a patient who had suffered from a prolonged and relapsing type of chorioretinitis. Organisms also were observed histologically in the chorioretinal lesions.

Results of our uveitis studies

We have conducted surveys on uveitis patients since 1947.* The following results have been obtained:

Methylene blue dye test

There were 1,230 samples of sera on which methylene blue dye tests were done, and in which complete studies on the patients were available. The sera were grouped according to the type of disease present in the eye:

I. Iridocyclitis
II. Chorioretinitis
III. Panuveitis
IV. Miscellaneous (eye diseases other than uveitis)

Table 5 is a composite of data from groups I, II, and III and shows the results of the methylene blue dye test in the various age groups. Thirty-five percent of sera were positive at a titer of 1:16 or higher.

The frequency of positive and negative tests in the various age groups can be estimated from the figures presented. It is known that the "normal" adult population in the geographic area represented by these tests shows about a 25 percent incidence of tests positive in a titer of 1:16 or more. It is difficult to draw conclusions about the incidence of active ocular toxoplasmosis from these figures. The higher incidence of positive tests in the uveitis group suggests that toxoplasmosis plays an important part in the etiology.

The subgroups represented in this chart are shown in Figures 16, 17, and 18, which show the titers in patients with iridocyclitis,

* I am indebted to Dr. Phillips Thygeson and Dr. Samuel Kimura for their advice and assistance in preparation of this paper. The three of us have collaborated for 10 years in operation of the Uveitis Clinic at the University of California School of Medicine, and we have seen all patients included in the survey. We are also indebted to many ophthalmologists on the Pacific Coast, too numerous to mention here, for their co-operation in sending cases for survey, and furnishing information on the follow-up care.

TABLE 5

DISTRIBUTION OF DYE TEST TITERS ACCORDING TO AGE OF PATIENT IN 1,072 CASES OF UVEITIS (ALL TYPES)

DYE TEST TITERS	0	5	10	15	20	25	30	35	40	45	50	55	60	65	70	75	80	85
1:4096	1		1						1				1					
1:1024	2					2	4	3	2	4	3	1	1					
1:256		2	1	3	3	6	9	4	8	7	5	1	3	3	1			
1:64	1	4	8	13	13	14	10	15	9	14	11	7	2	3				1
1:16		1	6	10	18	19	27	20	12	18	9	12	7	4	2	1		
Neg.	3	19	20	23	62	82	88	86	85	77	55	41	24	22	7	3	2	

AGES BY YEARS

chorioretinitis, and the miscellaneous (control) groups. The incidence of positive tests in the chorioretinis group is 50 percent and the titers tend to be higher than in the iridocyclitis and miscellaneous groups.

Toxoplasmin test and methylene blue dye test: Comparative analysis

The correlation of the skin and dye tests in various types of uveitis and in the miscellaneous groups are shown in Figures 19, 20, 21, 22, and 23. They confirm the results previously presented by our group. Of 617 patients with uveitis, 198 (32 percent) had positive dye tests and 141 (23 percent) had positive skin tests. Eighteen and one-half percent had positive dye tests at 1:16 or higher and negative skin tests. We have always considered the skin test as positive only when there are 10 mm. or more of induration at the end of 48 hours. Also, it is probable that some dye tests would be positive in a titer lower than 1:16. The correlation, therefore, might be closer if other cri-

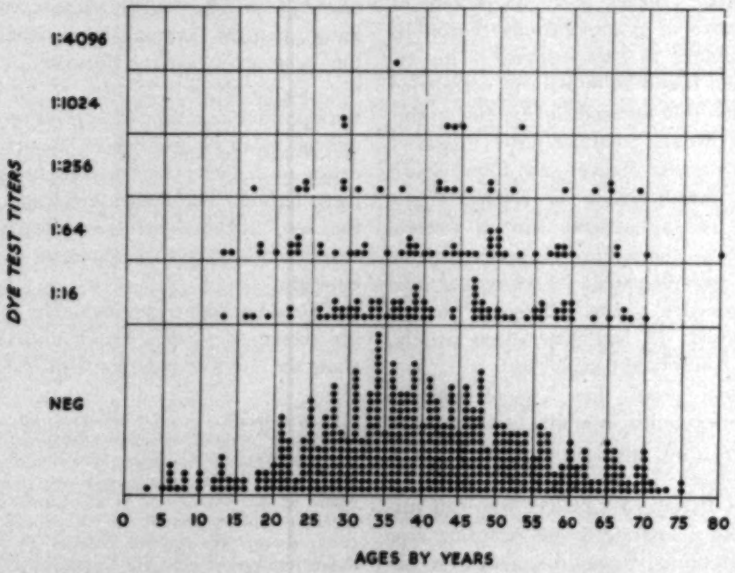

Fig. 16 (Hogan). Distribution of dye test titers according to age of patient in 649 cases of iridocyclitis.

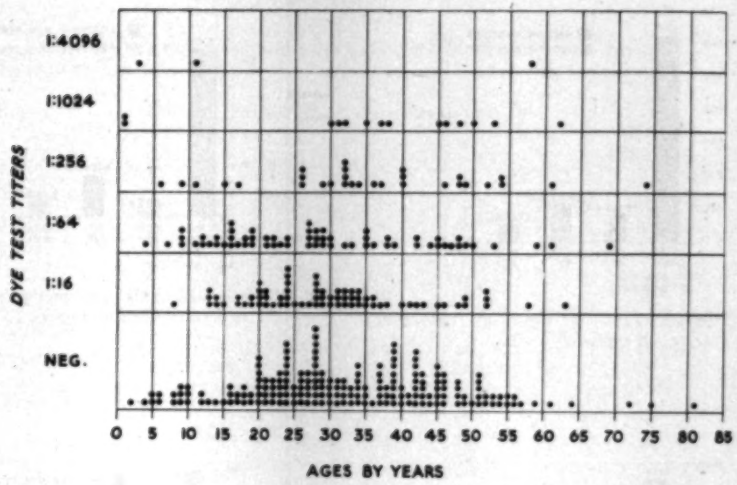

Fig. 17 (Hogan). Distribution of dye test titers according to age of patient in 375 cases of chorioretinitis.

teria were accepted. Other observers have found this to be so. It is less easy to explain the group consisting of 9.3 percent of the patients who had a positive skin test and a negative dye test. Possibly serum titers at lower levels were present.

The incidence of positive skin (36 percent) and methylene blue dye (48 percent) tests is considerable higher in the chorioretinitis group than in the other forms of uveitis and miscellaneous groups. The incidence of positive tests in the iridocyclitis group is about the same as that found in the general population. Figure 24 is a composite of the chorioretinitis and iridocyclitis groups to show the comparative frequency of positive dye and skin tests in the two groups. This study, too, suggests that a certain proportion of chorioretinitis patients have ocular toxoplasmosis.

Comparative skin test and dye test findings

Table 6 presents the results of all types of skin tests and the dye test in 1,241 uveitis cases. It is interesting that the frequency of positive results on the toxoplasmin test is

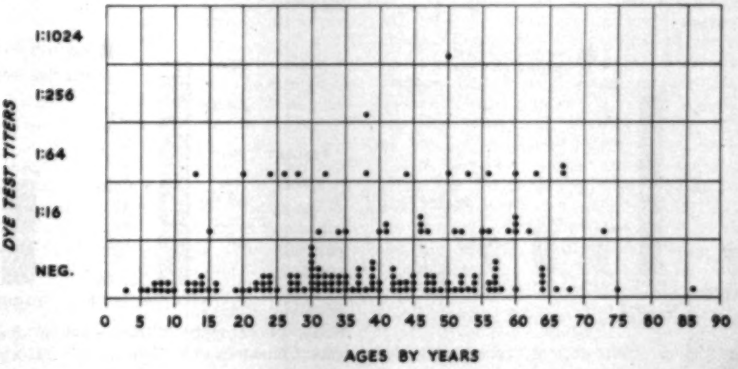

Fig. 18 (Hogan). Distribution of dye test titers according to age of patient in 158 miscellaneous cases.

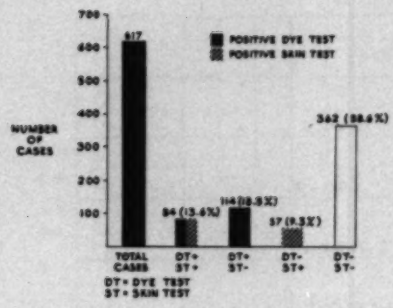

Fig. 19 (Hogan). Skin and methylene blue dye tests, all types of uveitis.

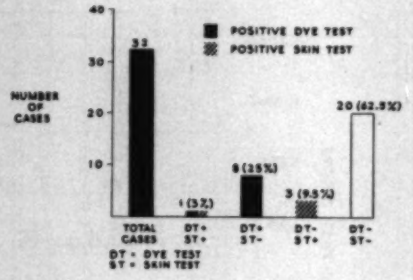

Fig. 22 (Hogan). Skin and methylene blue dye tests, diffuse uveitis.

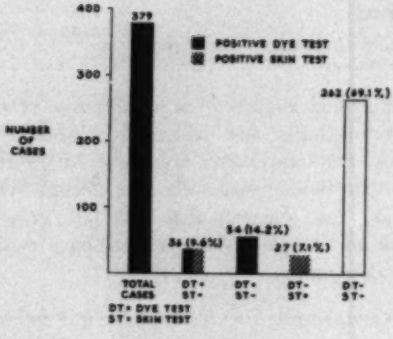

Fig. 20 (Hogan). Skin and methylene blue dye tests, iridocyclitis.

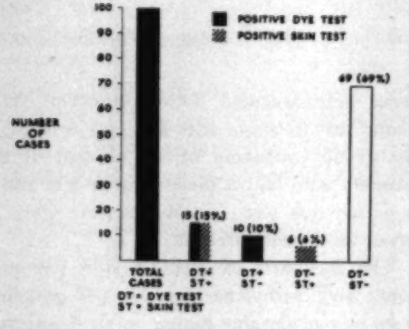

Fig. 23 (Hogan). Skin and methylene blue dye tests, miscellaneous.

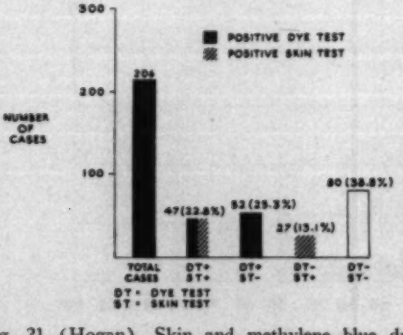

Fig. 21 (Hogan). Skin and methylene blue dye tests, chorioretinitis.

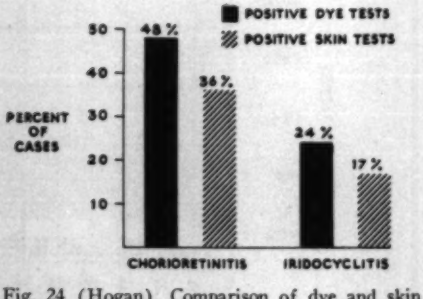

Fig. 24 (Hogan). Comparison of dye and skin tests. Chorioretinitis (206 cases). Iridocyclitis (379 cases).

TABLE 6

SKIN AND SEROLOGIC TESTS IN 1,241 CASES OF UVEITIS AND OTHER EYE DISEASES

	Skin							Serology
	PPD	Bruc.	Frei.	Coccid.	Toxo.	Histo.	All Skin Tests Neg.	DT 1:16 or Higher
C-R (386)								
Number	161	57	36	39	157	74	76	168
Percent	41	15	9	10	40	19	19	43
I-C (670)								
Number	312	239	60	71	122	75	195	151
Percent	46	35	8	10	18	11	29	23
Diffuse uveitis (57)								
Number	28	15	5	9	14	7	16	19
Percent	49	26	8	15	24	12	28	35
Miscellaneous (128)								
Number	71	19	6	6	37	20	31	34
Percent	55	14	4	4	28	15	24	26

as high as that on the tuberculin test in the chorioretinitis group, but that the incidence of positive results on the toxoplasmin test drops to 18 percent in the iridocyclitis group, although positive results on the tuberculin test remain at 46 percent.

CASE REPORTS

The following cases have been selected as interesting examples of the problems involved in the diagnosis of uveitis and toxoplasmosis. Some have been chosen to illustrate the results of treatment.

CASE 1

L. R., age 51 years, white man missionary.

I am indebted to Dr. C. P. Haseltine, Beaver Clinic, Redlands, California, for permission to present the findings in this unique case.

History. The patient was working in Peru in November, 1953, when the symptoms of malaria appeared. He developed chills, headache, fever, and anorexia. This continued for a week, at the end of which time he first consulted a physician. He was placed in bed and given intravenous fluids. Blood smears for malaria were positive. He was treated with Camoquin hydrochloride, which stopped the fever and chills. His convalescence was prolonged, and he had a disturbance of gait which persisted to the time when we first saw him (November, 1954).

Two weeks after onset of the general illness, vision in the right eye became blurred and impeded by many floaters. At this time the patient developed a severe cough and was told that he had a virus pneumonia. The vision gradually became worse, and two weeks later the blurring occurred in the left eye. Following the pneumonia he was very weak and failed to recover properly from his illness. In May, 1954, he was sent to Lima for ophthalmologic consultation. The diagnosis was bilateral chorioretinitis, and he was returned to the United States for treatment.

Prior to the onset of this illness the patient was exposed to insects (800 ft. altitude), but there were very few mosquitoes. He was working with a mule and some cattle, but they appeared to be healthy. The wife of another missionary had had several attacks of pneumonia while they were stationed at the mission.

At the first examination the vision in the right eye was 20/200 and in the left eye, 20/40. There was a moderate bilateral iridocyclitis. The right fundus showed a very large area of chorioretinitis superior to the disc, and a smaller one in the temporal periphery. The left fundus showed a large area of chorioretinitis superior to the disc, extending into the nasal and temporal portions of the fundus. Complete studies failed to reveal a cause for the illness or for the chorioretinitis. In November, 1954, blood was sent to us for a dye test. The result was position in a titer of 1:32,768. The complement fixation test was positive at a dilution of 1:64. A complete uveitis survey by our group in late November, 1954, failed to reveal any other cause for the ocular disease. The right aqueous humor had a dye test titer of 1:16. By this time the general condition of the patient was excellent, and the general physical examination showed no abnormalities.

Course: Table 7 and Figure 25 show the clinical and laboratory findings on this patient and his treatment during the subsequent 15 months. Treatment with Daraprim and sulfadiazine seemed to improve the ocular inflammation at first, and there was a temporary drop in the methylene blue dye test titer.

TABLE 7

ACQUIRED TOXOPLASMIC CHORIORETINITIS
PATIENT L.R., AGED 51 YEARS, WHITE MALE

Dec. 1953	Jan. 1954	Feb. 1954
Malaria, followed in 2 wk. by cough, and bilateral chorioretinitis	Relapse malaria Chorioretinitis still active	Viral pneumonia Chorioretinitis still active

Nov. 1954

Vision	RE—20/200 LE—20/40
Fundi	RE—3+Coarse and fine vitreous opacities. Chorioretinitis superiorly and temporally LE—3+Vitreous opacities. Large Chorioretinitis above disc

Dye Test 1:32,768

Continued therapy failed to help, and there were exacerbations and remissions in the ocular inflammation. The patient was then given chloroquine, which seemed to result in improvement. Both the dye test titer and activity of the lesions decreased. Eventually there was complete healing. By March, 1956, vision in each eye was 20/20 and the patient returned to his missionary duties.

Comment: It is probable that the virus pneumonia which this patient had suffered subsequent to the malaria was really a toxoplasmic infection. It is interesting that the eye lesions came on at about the same time as the pulmonary infection. The persistence of high dye and complement fixation test titers in this patient for a year after onset of the pneumonia was of great value in the diagnosis. The low methylene blue dye test titer in the aqueous humor shows the lack of value of this test on aqueous humor. In view of the reported successful experimental and clinical studies on toxoplasmosis with Daraprim and sulfadiazine, it is difficult to explain the poor response of the eye disease to treatment.

CASE 2

M. D., aged 44 years, an army officer. (I am indebted to Col. Robert Kelley, Letterman Army Hospital, for permission to publish the findings on this interesting patient.)

History: In July, 1951, while in Cleveland, Ohio, this man developed a fever of 104° F., chills, and malaise, lasting about 21 days. He was treated at a

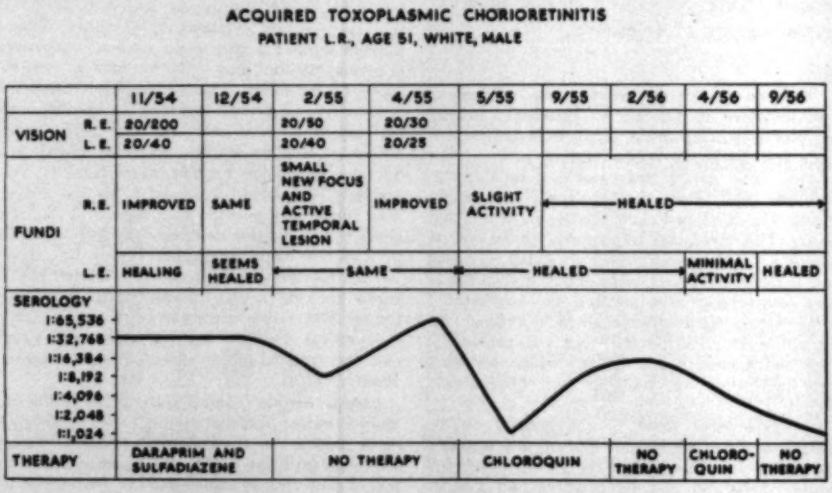

Fig. 25 (Hogan). Case 1, acquired toxoplasmosis.

Veterans Administration Hospital. The elevated temperature gradually returned to normal. At the time he was thought to have amebiasis, but no organisms were found. All other studies revealed no abnormality, including tests for brucellosis. He continued to have recurrent bouts of fever and chills following his transfer to the Army Hospital at Fort Sill. There were no pulmonary or skin lesions. About the first of November, 1951, the patient observed that vision in the left eye was becoming cloudy, and a diagnosis of chorioretinitis was made. His visual acuity was 20/50 and there was a six-degree scotoma (2/1,000) just below fixation. He was treated with cortisone, streptomycin, penicillin, Aureomycin, and emetine, and was discharged from the hospital in January, 1952, much improved. The eye condition and fever recurred in March, 1952, and again in September, 1952. After this the vision was recorded as 6/200. While this man was in Austria in February, 1953, there was a recurrence. In January, 1957, he had a relapse and was seen at Letterman Army Hospital, San Francisco.

Examination: In January, 1957, general physical examination showed no abnormalities. Vision in the right eye was 20/20 and in the left, 3/400. The right eye was normal. The left cornea showed some nonpigmented fine white keratic precipitates and there was a mild iridocyclitis. The left vitreous showed a moderate number of coarse and fine opacities. There were old healed flat chorioretinal scars in the extreme periphery at the 4-, 8-, and 11-o'clock positions. The macular and perimacular areas showed scarring with some pigmentation covering an area of approximately one disc diameter. The patient was kept in the hospital for 20 days; the vitreous gradually cleared and the iridocyclitis disappeared.

A complete uveitis survey was repeated by us on June 11, 1957. A moderately positive reaction followed the first test dose of purified protein derivative (PPD), and strongly positive histoplasmin and toxoplasmin reactions were obtained.

Laboratory findings: The following positive methylene blue dye test titers were obtained:

2/1/57 1:1,024
3/27/57 1:8,192 (almost positive at 1:16,384)
6/11/57 1:32,768

Course: In view of the quiescence of the ocular lesions, further treatment was not recommended. There have been no further recurrences of the eye symptoms or of the systemic condition (August, 1957).

Comment: The close relation between the systemic illness and development of the ocular condition indicates that they were due to an identical etiologic agent. The failure to find a specific cause of the patient's illnesses in 1951 and 1952 suggests that he had had an active toxoplasmosis. The recurrences of his ocular disease also suggest such an infection. The diagnois was confirmed by the high and rising titer in the serologic tests.

CASE 3

F. G., aged 53 years, white housewife. (I am indebted to Dr. Ulrich Fritschi of Sacramento, California, for permission to study and publish the results of investigations on this patient.)

Chief complaint: Blurred vision, right eye, 10 months.

History: The right eye became inflamed and the vision blurred in April, 1955. There was very little pain. Examination showed large mutton-fat keratic precipitates, posterior synechias, many cells, and a dense flare in the anterior chamber. The pupil was dilated with difficulty and the fundus could be seen very poorly. Detailed laboratory and physical studies failed to reveal a cause for the uveitis. Within a few months after onset of the uveitis, the patient developed a rapidly progressive cataract. Because of failure of the disease to respond to streptomycin, Promizole, and hydrocortisone, the patient was referred to us for further evaluation.

Past history: The patient had poor vision and an exotropia of the left eye for many years. This eye had never been inflamed.

Examination: The right eye had fair light perception but poor projection. The intraocular pressure was normal, the cornea was clear, and there were old crenating mutton-fat keratic precipitates. The aqueous showed two-plus flare and cells. The iris stroma was atrophic, and there were scattered posterior synechias. The lens was completely cataractous. The left eye had 20/70 vision and a high refractive error, and there was an inferior conus of the optic disc.

General physical examination and detailed laboratory studies failed to reveal a cause for the uveitis other than a probable toxoplasmosis.

Laboratory studies: Results of all skin tests were negative except that for toxoplasmin, which was strongly positive. The methylene blue dye test on the serum was positive in a titer of 1:1,024 and the aqueous humor titer was 1:128, which is unusually high. Subsequently the complement fixation test changed from negative to positive at a 1:10 dilution. Cultures of aqueous humor in tissue culture, fertile eggs, and on HeLa cells were negative

Course: The patient was given a course of Daraprim and sulfadiazine by mouth, and the inflammation eventually cleared. We could not say whether a definite therapeutic response was obtained. A cataract extraction was done on the right eye in the latter part of 1956, and the patient was referred for further studies in March, 1957. The results of the cataract extraction were excellent, but the upper fundus of the right eye showed a tremendous area of healed chorioretinitis, extending from the disc to the periphery and resulting in preretinal veiling and obscuration of the macular area.

Comment: The severity of the lesion in the fundus, granulomatous nature of the anterior ocular inflammation, rapidly progressive cataract, absence of other possible causes of the disease, and significantly positive serologic and aqueous humor studies

point to this case as being one of ocular toxoplasmosis.

CASE 4

F. H., aged 32 years, white waitress.

Chief complaint: Blurred vision, one month.

History: Blurred vision developed in the left eye about the middle of September, 1955. This was associated with pain in the eye and periorbital region. The patient was sent by her physician to an ophthalmologist who prescribed atropine, cortisone drops, and tetracycline by mouth. These failed to cause improvement, and she was referred for further studies.

Past history: Early in 1955 the patient had been treated for a rather severe spastic colitis. No other disease could be related to the present episode. Her mother had developed tuberculosis when the patient was five years old, but results of follow-up tests in this patient were always normal.

Examination: During October, 1955, the patient's vision was 20/20 in the right eye, and there was no evidence of disease. The visual acuity in the left eye was 20/100. There were one-plus congestion, three-plus flare, and one-plus clot in the anterior chamber. There were no keratic precipitates. Fundus examination showed four-plus vitreous opacities and a very large area of chorioretinitis in the lower nasal portion.

Laboratory studies: The reaction to the second test dose of PPD) was positive, and the toxoplasmin skin test was markedly positive. The methylene blue dye test was positive in a titer of 1:64, and the complement fixation test was positive at 1:10. The sedimentation rate was elevated to 30 mm., corrected (Wintrobe). General physical examination revealed no abnormalities.

Course: Further dye tests during 1955 and 1956 showed the methylene blue dye test titer to range between 1:64 and 1:256. In April, 1956, the titer rose to 1:1,024. During 1957 the titer remained fairly constant at 1:256 and results of the complement fixation tests were negative.

The patient was treated with chloroquine during November and December, 1955, without effect on the ocular inflammation. Gradual clearing occurred by mid-January, 1956, but about this time a new lesion appeared just above the old one. This new focus gradually cleared, and in February, 1956, the patient had vision of 20/30 in the affected eye, and only one-plus flare and cells in the aqueous humor.

The disease finally became quiescent and remained so until March, 1957, when a severe acute relapse occurred. The visual acuity in the left eye was reduced to hand movements, and three-plus cells and flare were seen in the aqueous humor. There were small white keratic precipitates. The patient was given Daraprim 75 mg. a day, sulfadiazine two gm. a day, and Meticorten 15 mg. a day. Fairly rapid improvement occurred, so that one month later the visual acuity was 20/70 and there was a plus-minus flare and cells in the anterior chamber. The vitreous continued to show about three-plus cells and there was questionable activity in the chorioretinal lesion.

Comment: This case illustrates the difficulties involved in the diagnosis of possible toxoplasmosis. The low initial dye test titer in this patient's blood might have made the diagnosis of ocular toxoplasmosis questionable. However, the increasing titer, development of a positive complement fixation test, and rapid response to Daraprim and sulfadiazine present strong evidence in favor of a toxoplasmic origin.

CASE 5

M. S., aged 48 years, housewife. (I am indebted to Dr. Dohrmann Pischel for permission to present the findings in this case.)

History: In May, 1951, the patient developed discomfort in the left eye, followed by congestion, blurring, and photophobia. This was treated, and over a period of six weeks it gradually cleared, but there was some residual blurring. In October, 1951, there was a recurrence, persisting to March, 1952, when we first saw the patient. Examination at that time showed that the right eye was entirely normal and that the left eye had 20/50 vision with one-plus congestion, three-plus cells and flare in the anterior chamber, two-plus fine anterior vitreous opacities, and a rather large, very indistinct area of yellowish chorioretinitis along the superior temporal vessels. The patient was treated with cortisone, diathermy, Omnadin, and atropine, and the lesion gradually cleared.

In October, 1952, there was a relapse. At this time a survey showed only a positive tuberculin test result in the first test dose of PPD. Results of toxoplasmin skin test and the methylene blue dye test were negative. The erythrocyte sedimentation rate (corrected) was 25 mm. (Wintrobe), and the white blood count was 10,400 per cubic millimeter. An explanation for the elevated sedimentation rate was not found. It was recommended that a biopsy of a neck gland be obtained (not done), and that the patient be treated with streptomycin and para-aminosalicylic acid. This was done and the disease gradually quieted, but the patient was left with very blurred vision. Subsequent exacerbations and remissions occurred.

We saw the patient again in February, 1957, because of continued relapses. She was hospitalized, and a complete survey was repeated. The skin tests still showed a positive tuberculin reaction and a positive reaction to brucellergin. The toxoplasmin skin test was negative. The sedimentation rate was normal. Physical examination and other laboratory studies failed to show any abnormality except the methylene blue dye test titer, which was now 1:256 and arose to 1:1,024 a month later. During the next five months the dye test titers were 1:256. The complement fixation test remained negative.

In August, 1957, the right eye was normal. The left eye had only light perception and the cornea was quite hazy because of epithelial edema and a massive deposition of large mutton-fat keratic pre-

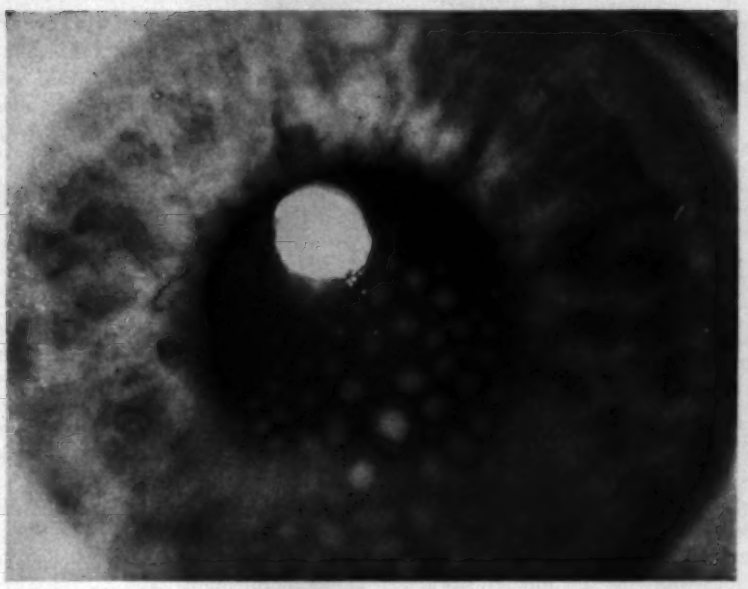

Fig. 26 (Hogan). Acquired ocular toxoplasmosis, severe anterior inflammation with mutton-fat keratic precipitates.

cipitates on the lower two thirds of the cornea (fig. 26). There were four-plus cells and flare in the anterior chamber, extensive posterior synechias, a number of nodules in the iris stroma, and cataractous changes in the lens. The vitreous and fundus could not be seen, although light projection was fairly good.

Past history: In 1929, the patient had developed persistent diplopia. In 1934, she had had a left optic neuritis for two months with complete clearing. A recurrence of the neuritis occurred in 1948, and the vision was decreased for six weeks. She was told that it was possible that she had multiple sclerosis, but further symptoms of this disease have failed to develop. Other than several psoriatic lesions on her legs, she had always been healthy.

Course: The accompanying graph (fig. 27) shows the course of the disease and the treatment insti-

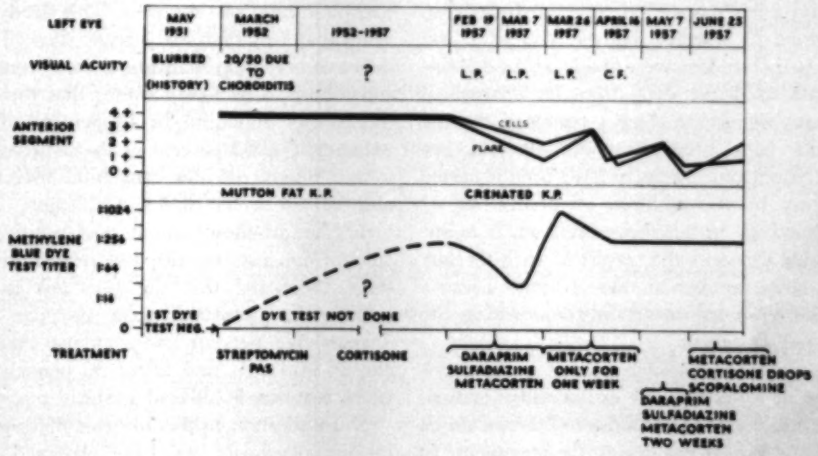

Fig. 27 (Hogan). Case 5, acquired toxoplasmosis.

tuted for this patient. The response to Daraprim and sulfadiazine and Meticorten was excellent, and at the present time only very low grade activity can be seen in the anterior segment.

Comment: The reversal of a previously negative dye test to one which was positive is evidence of a toxoplasmic infection. The failure to respond to antituberculous drugs, and the fairly prompt response to sulfadiazine and Daraprim would tend to confirm our opinion that this is an example of ocular toxoplasmosis.

Therapy of toxoplasmosis

Early studies showed an in vitro and in vivo sensitivity of Toxoplasma to sulfonamides and to some antimalarials. Subsequent clinical studies in humans with these drugs and chemicals were disappointing. Eyles and Coleman[7] later showed that Toxoplasma infections in experimental animals were responsive to combinations of sulfadiazine and pyrimethamine (Daraprim), an antimalarial, and that these combinations were synergistic in their action. Ryan and co-workers[29] showed that these drugs were effective in human ocular toxoplasmosis. This was confirmed by Perkins and co-workers.[26]

Since the reports of Eyles, we have employed these chemicals, individually and in combination, in a fairly large series of patients. A number were given these medications in appropriate doses for two to three weeks. The treatment was usually carried out for a five day period, with a two day rest, followed by another five day course. Blood and urine studies were made at weekly intervals to detect drug toxicity. Occasional patients seemed to show a response, but the results have been disappointing. An improved outcome seems to have been obtained recently by the addition of prednisone or prednisolone to the above regimen. It is impossible to assess the results of such therapy in a large number of these patients because of the frequent uncertainty concerning the original diagnosis.

In six patients with almost certain evidence of a toxoplasmic ocular inflammation, only one showed a response to therapy which could be considered due to the treatment. In 12 other patients, some with evidence of a late relapse of a congenital infection or with probable acquired ocular disease, only three gave prompt response to this therapy. It should be noted that one fairly definite case (Case 1) of acquired ocular toxoplasmosis reported in this paper failed to respond. It is not surprising that such chronic or long-standing cases should fail to respond to the medication, because the inflammatory exudate and reaction to the inflammation might prevent access of the drug to the organisms. These therapeutic studies can be summed up by saying that the outcome often was disappointing.

Summary and Conclusions

1. The acute manifestations of congenital toxoplasmosis are well established and include chorioretinitis, encephalomyelitis and visceral inflammation.

2. Ocular toxoplasmosis may be overlooked in an apparently healthy child until attention is directed to the eyes by the development of a strabismus, by detection of amblyopia in one or both eyes during a routine eye examination, or by the development of increased blurring due to a late relapse of the chorioretinal inflammation.

3. Thirty-six cases of congenital ocular toxoplasmosis are reported. This study reveals that less than 20 percent showed evidence of cerebral calcification which could be considered to be toxoplasmic; that the condition was unilateral in 30 percent of the patients; that 33 percent of the patients had a late relapse of the congenital infection; and that 55 percent had a strabismus.

4. Nine of these patients had positive results of dye tests and negative results on skin tests, indicating that the skin test is less reliable for diagnosis than the dye test. Twenty-five percent had dye test titers in excess of 1:512, and about 36 percent had titers between 1:128 and 1:512.

5. In addition to the 36 cases of congenital toxoplasmosis, we have observed four

others with a late relapse of congenital toxoplasmic infections. Toxoplasma was isolated from the enucleated eye of one of these patients 20 years after birth.

6. Ocular inflammation rarely occurs during the course of acute postnatally acquired systemic toxoplasmosis, although some cases have been reported.

7. In uveitis cases, questionable enlarged lymph nodes should be excised for microscopic and cultural studies.

8. The methylene blue dye tests on patients with uveitis in various age groups showed 35 percent of the sera to be positive in a titer of 1:16 or higher. This can be compared to a 25-percent incidence in a miscellaneous group of nonuveitis cases.

9. The correlation of results of the methylene blue dye test and the toxoplasmin test in 617 cases of uveitis revealed that in 32 percent results of dye tests were positive and in 23 percent results of skin tests were positive. Forty-eight percent of patients with chorioretinitis reacted positively to dye tests and 36 percent reacted positively to skin tests. This can be compared with 25 percent and 18 percent of the normal population in this area.

10. The various skin tests in 1,241 cases of uveitis and in a miscellaneous group disclosed that approximately 40 percent of the patients with chorioretinitis and 18 percent of the patients with iridocyclitis had positive reactions to toxoplasmin tests. In this same group, 43 percent of those with chorioretinitis and 23 percent of those with iridocyclitis had positive dye test titers. The percentage of incidence of positive dye and skin tests in the iridocyclitis group was the same as in the control group.

11. In the cases studied there were five of acquired adult ocular toxoplasmosis. Two of these were associated with acute systemic infections.

12. Daraprim and sulfadiazine therapy of acquired ocular toxoplasmosis was found to be disappointing, but further studies seem to be warranted.

University of California Medical Center (22).

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THE ADHESION OF THE LENS CAPSULE TO THE HYALOID MEMBRANE*

And its relation to intracapsular cataract extraction

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A great deal of attention has been given to the role which the zonules play in fixing the lens. There is little in the literature on the part played by adhesions between the anterior hyaloid membrane and the capsule in securing the lens.

Wieger[1] first described the occurrence of some degree of normal adhesion of the lens capsule to the hyaloid and gave it the name ligamentum hyaloideocapsulare. However, Duke-Elder[2] felt that this attachment is of little clinical importance. Goldsmith[3] observed the adhesion of the hyaloid to the lens capsule, and Vail[4] in his excellent discussion stated: "The posterior capsule of the lens is closely connected with the anterior surface of the vitreous through capillary attraction in the retrolental fossa, to adhesions formed by the ligamentum hyaloideocapsulare, by embryonic fibers joining the posterior lens capsule to the anterior hyaloid, or by all three."

Vail[5] also states:

> The smooth, moist convex surface of the lens is in intimate contact with the smooth, moist concave surface of the anterior hyaloid membrane, in Berger's[6] retrolental space, the latter, however, being only potential. There is, therefore, capillary attraction, which is strong. In addition, if the ligamentum hyaloideocapsulare of Wieger is an actual structure, and there is evidence that it is, then there is an actual adhesion between the posterior capsule of the lens and the hyaloid membrane. In addition, there is evidence that embryonic adhesions may also be present. Thus, a rough pull upon the lens can tear the anterior hyaloid membrane and produce characteristic holes, seen many times with the biomicroscope after operation, and lead to herniation of vitreous mass into the anterior chamber.

Our attention was directed to the adhesions between the capsule and the hyaloid at the time of operation on supposedly uncomplicated cataracts. When such an "adhesion syndrome" was noted at the time of an extraction, we made it a practice to section the lens to see if we could detect any hyaloid elements which were adhering to the posterior capsule. Figures 1, 2, and 3 are examples of the findings we encountered. Bellows[7] states that the presence of the pigmented ring on the posterior lens surface is due to pigment in the patellar fossa after injury or inflammation. Its ring shape is due to the normal adhesion of the lens to the anterior hyaloid.

After extracapsular extractions on three eyes in which the lens remained firmly adherent to the hyaloid, even when the zonules were obviously ruptured, there was noted postoperatively an opaque circle with a clear center on the face of the vitreous (fig. 4). This circle represents, in our opinion, firm adhesion between the capsule and the hyaloid at the site of the ligamentum hyaloideocapsulare.

In an attempt to determine the extent of the adhesion between the capsule and the hyaloid and its possible significance in cataract extraction, we performed extractions on 20 fresh eyes which we believed to be normal or at least normal for our purposes in the anterior sector.[8] Among the 20 eyes available, nine had melanomas of the choroid. The other 11 were obtained at autopsy or because of an exenteration for an orbital new growth. In each eye the cornea was excised and the iris removed at its base, thereby exposing the lens and its zonular membrane. The lens was then grasped with Arruga forceps, and by gentle traction it was removed in its capsule. In 15 (75 percent) of the eyes the zonular membrane rup-

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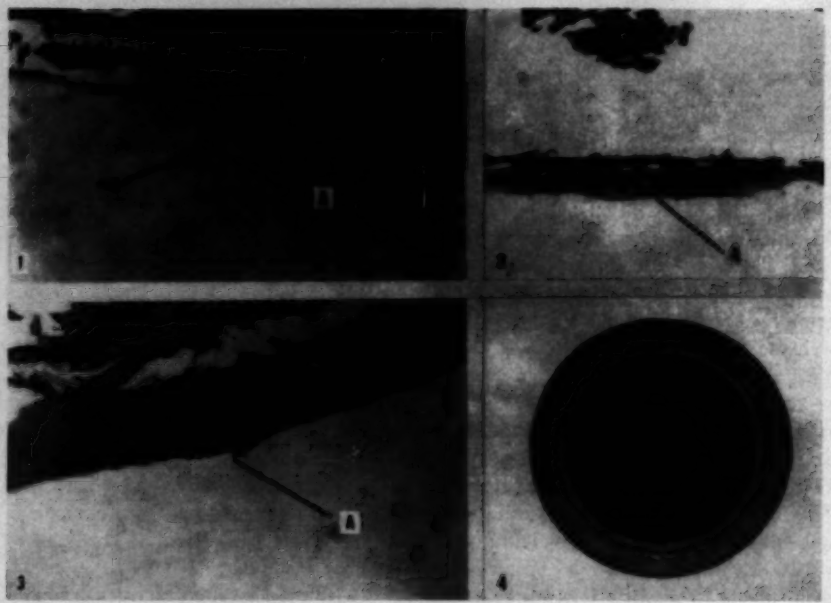
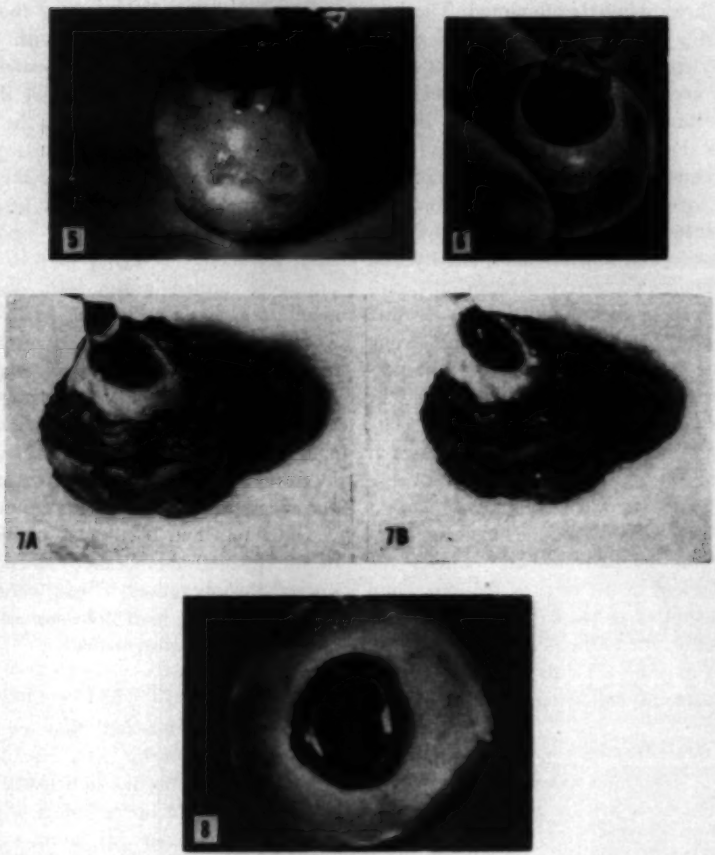


Figs. 1 to 4 (Reese and Wadsworth). (1) This photomicrograph of an adherent lens removed in capsule shows a splitting of the posterior capsule (A) or a lamination of the hyaloid membrane adherent to the capsule. (2) An adherent lens removed in capsule shows a thickened posterior capsule (A). Scattered pigment granules are present. (3) An adherent lens removed in capsule shows a cellular deposit with pigment granules on the posterior capsule. There is also an irregularity in the thickness of the capsule. This patient had iritis a number of years previous to extraction. (4) An opaque circle with a clear center on the face of the vitreous representing adhesion between the capsule and the hyaloid at the site of the ligamentum hyaloideocapsulare. The sketch was made on the 14th day following an extracapsular extraction of a lens which was too firmly adherent to the hyaloid to permit an intracapsular extraction.

tured, easily permitting the lens to be delivered without evidence of any adhesion of it to the vitreous (fig. 5). In five (25 percent) of the eyes studied the hyaloid was so firmly adherent that it came forward with the lens after the zonular membrane was broken. When the capsule was peeled off, the hyaloid snapped back to its normal position. The various degrees of adhesion between the hyaloid and capsule are shown in Figures 6, 7A, and 7B. When the adhesion was firm, the lens could be drawn far away from the globe before the hyaloid separated; and, in one instance, the adhesion was so firm that a round, punched-out hole was left in the hyaloid (fig. 8).

It is possible that an adhesion of the hyaloid and capsule may be fostered by a previous inflammation, and we have some evidence to support this. In Figures 3 and 4 we see what seems to be evidence of sequelae from a previous iridocyclitis. Furthermore, several times when extracting a cataract complicating a past iridocyclitis, we have noted firm adhesions between the capsule and the hyaloid; in one eye the adhesions were so firm that the two structures could not be separated.

More often, though, the adhesion seems to be on a developmental basis. As the primary vitreous and the tunica vasculosa lentis disappear with the development of the secondary vitreous, small remnants of the mesodermal tissue may remain along the posterior capsule of the lens.[9] At about the same time the zonular membrane (tertiary vitre-



Figs. 5 to 8 (Reese and Wadsworth). (5) Experimental cataract extraction with lens delivered without evidence of adhesion to the hyaloid. (6) A drawing of an experimental cataract extraction demonstrating adhesion of the lens to the hyaloid. (7) Experimental cataract extraction showing adherence of the capsule to the hyaloid. (A) and (B) are different stages in the same extraction. (8) A punched-out round hole in the hyaloid following experimental extraction of an adherent lens.

ous) develops from the ciliary epithelium and extends to encompass a portion of the lens capsule. At the junction where the secondary vitreous and the zonular membrane meet there may be remnants of the mesodermal tissue from the primary vitreous or tunica vasculosa lentis.[10] Fusion of these three layers with the posterior lens capsule occurs at the ligamentum hyaloideocapsulare (Eggers' line).[11] We have not been able to detect, with the biomicroscope, adhesions between the two structures at the so-called ligamentum hyaloideocapsulare. Redslob[12] believes that small fibers extend from the posterior lens capsule into the vitreous.

An undue adherence of the hyaloid to the capsule may manifest itself in several ways at the time of the cataract extraction. First, the surgeon appreciates the presence of adhesions when the lens remains deep in the eye and does not show a tendency to come forward, either as a whole or at the equator

below, if a tumbling is attempted. The lens tends to slip behind the posterior lip of the wound. When the zonules at the lens equator below are obviously broken, the lens still will not tumble or present itself in the wound, or the lens hangs in the wound even with the equator presenting. When the lens is teased forward with the forceps, one can sometimes see the hyaloid peel off the posterior capsule of the lens. After the hyaloid finally becomes completely free of the capsule, one feels or sees the vitreous body sink back suddenly. If the adhesion is too strong to separate the two structures and one perseveres with forceps, the capsule may be broken or vitreous lost. Failure to appreciate the adhesion between these two structures at the time of extraction is one important cause of capsule rupture or vitreous loss.

The adhesion between the posterior capsule and the hyaloid probably causes the pull on the lens at the time of the extraction to be transmitted to the base of the vitreous which is adherent to the periphery of the retina. This may be a factor in producing retinal detachment following cataract extraction.

When this adhesion syndrome is appreciated, it is sometimes possible to tease the two structures apart by wedging a spoon between the hyaloid and the capsule with the cornea intervening.

The difficulty of separating the adhesion between the two structures with forceps is that the lens cannot be adequately everted without so stretching the capsule that it ruptures. This can be obviated by the use of an erisophake. We believe the erisophake has particular virtues in combating this adhesion syndrome. The instrument can be rotated so that the lens can be gradually, and if necessary completely, everted and in this way gradually peeled away from the hyaloid membrane. Even when the lens lies in the wound and is practically delivered, the last remaining adhesions between capsule and hyaloid may be sufficiently strong to tear a hole in the hyaloid if delivery is done precipitously.

Vannas[13] found that eight percent of eyes on which intracapsular extractions without vitreous loss had been done showed a tear in the hyaloid membrane immediately following the operation. These were probably rents caused by firm adhesion of the ligamentum hyaloideocapsulare.

Summary

Evidence is presented that an adherence between the posterior lens capsule and the anterior hyaloid occurs sufficiently in degree and frequency to be reckoned with in performing an intracapsular cataract extraction.

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AQUEOUS HUMOR DYNAMICS*

The effect of pentolinium (Ansolysen) on normal human eyes

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Introduction

The purpose of this paper is to report the failure of a ganglionic blocking agent, pentolinium (Ansolysen), to alter aqueous humor dynamics in normal human eyes.

Method

The patients selected were young, healthy subjects without eye pathology. Their average age was 20.6 years. On the control day one or two tonograms without medication were obtained in order to train the patients for the procedure. At least two days later Goldmann applanation tonometry and control tonographic tracings were carried out. The patients were given 20 mg. of Ansolysen by mouth and approximately one and a half hours later the applanation readings and tonography were repeated in identical fashion. The right eye was always examined first.

Tonography was performed with a Mueller electronic tonometer linked to a Leeds and Northrup Model B Speedomax Recorder.

For estimation of intraocular pressure (P_o) and outflow facility (C) values Friedenwald's 1955 calibration tables were used with suitable corrections.[1] Aqueous flow rates (F) were calculated from the equation $F = C\ (P_o - 10)$. To obtain scleral rigidity values the applanation readings and Schiøtz hand tonometer measurements with a 5.5 gm. weight were compared and plotted on Friedenwald's nomogram.

Results

The results of the effects of Ansolysen administration are summarized in Table 1. No significant changes in intraocular pressure, rate of aqueous flow, or scleral rigidity coefficient were found. Ansolysen did not block the "ophthalmotonic consensual reaction," that is, the difference in opening pressure between the first and the second eye induced by tonography.

Similar experiments conducted without intervening medication were used to evaluate the effects of repeated tonography on normal human eyes. The results are summarized in Table 2. In these studies tonography was found to be remarkably reproducible. The figures resembled those in the Ansolysen experiments. The magnitude of the "ophthalmotonic consensual reaction" was about the same as observed by others.[2, 3]

Discussion

The effects of Ansolysen on experimental animals have been studied previously. Dev Paul and Leopold[4] reported that 10 to 20 mg. of Ansolysen caused a transient fall in intraocular pressure in rabbits. Bárány[5] gave rabbits twice as much Ansolysen and found no change in outflow resistance. In rabbit tonographic studies Becker and Constant[6] noted no changes in intraocular pressure or outflow facility.

In glaucomatous human eyes, Hexamethonium, another ganglionic blocking agent, is said to cause no change in outflow facility, but a transient decline in intraocular pres-

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TABLE 1

EFFECT OF ANSOLYSEN 20 MG. ON THE AQUEOUS HUMOR DYNAMICS IN 30 NORMAL HUMAN EYES[a]

	Control	Ansolysen
Intraocular pressure (P_0) (Applanation tonometric pressures)	14.9±2.12 mm.Hg	13.9±2.12 mm.Hg
Rate of aqueous flow (F)	1.69±0.91 μl	1.56±0.88 μl
Scleral rigidity coefficient (E)	0.0211±0.0059	0.0216±0.0039
Ophthalmotonic consensual reaction (ΔP)[b]	1.60±1.22 mm.Hg	1.26±1.45 mm.Hg

[a] All values expressed as mean ± standard deviation.
[b] Pressure difference between first and second eye subjected to tonography.

TABLE 2

REPEATED TONOGRAPHY IN 18 NORMAL HUMAN EYES WITHOUT MEDICATION[a]

	First Tonography	Repeated Tonography (1–4 hours later)
Intraocular pressure (P_0)	14.35±3.0 mm.Hg	13.45±3.6 mm.Hg
Rate of aqueous flow (F)	1.12±0.69 μl	1.00±0.63 μl
Ophthalmotonic consensual reaction (ΔP)[b]	1.45±1.70 mm.Hg	1.22±1.82 mm.Hg

[a] All values expressed as mean ± standard deviation.
[b] Pressure difference between first and second eye subjected to tonography.

sure.[7, 8] This was attributed to a decrease in aqueous formation. Iwata[9] found Ansolysen to cause a transient fall in intraocular pressure. With Ansolysen, Rosen[10] found differences in glaucomatous eyes before and after the administration of miotics. In untreated eyes the inhibition of rate of flow appeared to be less, and the outflow facility did not change appreciably.

In nonglaucomatous human eyes Ansolysen is reported not to effect the intraocular pressure.[11] In a series of patients treated with the ganglionic blocking agents, Ansolysen and mecamylaminhydrochloride (Mevasine), for their blood pressure, Linnér[3] noted no differences in intraocular pressure and outflow facility. Furthermore, in this series ganglionic blocking agents were not found to block the "ophthalmotonic consensual reaction" induced by tonography. However, Rosen[10, 12] reported an inhibition of aqueous flow up to 77 percent following Ansolysen administration to patients with normal eyes. The large fall in secretion was almost fully compensated by a decrease in the facility of outflow and pressure changes were small. In Rosen's series Ansolysen also inhibited the "ophthalmotonic consensual reaction" so that the pressure difference between the first and second eye after Ansolysen was consistently less than before therapy and even became negative. In the present study the findings of Rosen could not be confirmed.

SUMMARY

The effects of pentolinium (Ansolysen) on aqueous humor dynamics were studied by means of tonography and the Goldmann applanation tonometer. Twenty mg. of Ansolysen, given by mouth to young, healthy subjects, did not have any significant effects on the intraocular pressure, rate of aqueous flow, and scleral rigidity, nor did it block the "ophthalmotonic consensual reaction" induced by tonography. In trained subjects, repeated tonography proved remarkably reproducible.

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PRIMARY TUMORS OF THE ORBIT

With case reports

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Primary tumors of the orbit comprise a heterogeneous group of lesions which are encountered quite rarely by the average practicing ophthalmologist. This report is concerned primarily with experiences in treating a consecutive series of cases at the U. S. Naval Hospital, San Diego, California, over a five-year period. Only those cases which came to surgery are included. The incidence was one in every 15,581 clinic visits. It is not the intent of this paper to review the literature comprehensively, but to refer only to certain pertinent sources primarily pertaining to the surgical treatment.

When the ophthalmic surgeon is confronted with a patient exhibiting proptosis, and more particularly when it is unilateral, the diagnostic workup and observation period will usually be quite extensive and prolonged. The diagnosis by clinical methods is frequently impossible. The usual signs and symptoms are more general rather than specific, and there is much overlapping among the broad etiologic categories; namely, inflammatory, vascular, endocrine, and neoplastic. Duke-Elder[1] states that inaptitude with clinical methods is partially compensated by the fact that once a tumor mass is felt it should be attacked surgically. Therefore, after a complete diagnostic workup and an adequate observation period, surgical exploration is usually indicated.

Reese, Benedict, Davis, Krönlein, and others[2–4] have delineated specific approaches to the orbital tissues. These are well known

to all and should be adapted to each individual case depending on the findings, particularly the location of the tumor within the orbit. The very important question of when surgery should be done must be answered. Reese[2] has advocated certain criteria which we found to be most useful. They are partially summarized as follows:

Proptosis with a palpable mass

1. Mass well defined—appropriate surgery
2. Mass ill defined—modified Krönlein approach of Reese

Proptosis without a palpable mass

1. Visual function impaired—modified Krönlein
2. Retinal striae present—modified Krönlein
3. No pertinent findings—temporize and observe

Definitive treatment must await the report of the histopathology. The proper surgical approach will give us that and many times result in a cure by simple excision of the tumor mass. If a well-defined, encapsulated tumor mass is found, complete excision is indicated. When the mass is ill defined, friable, or invasive, a biopsy should be taken and additional measures instituted as dictated by the cell type.

As found by Reese,[3] 90 percent of primary orbital tumors fall into eight pathologic groups. These are, in order of frequency: hemangioma, dermoid cyst, lymphomatous tumors, pseudotumor, meningioma, glioma of the optic nerve, mixed tumor of the lacrimal gland, and peripheral nerve tumors. In the large series reported by Ingalls,[6] there are some slight variations with retinoblastoma taking the place of glioma of the optic nerve. This is probably explained by the unusual age group in his cases. In our experience with seven consecutive cases, five of these categories were represented, one of them twice. One case, cyst of the lacrimal gland, fell into a less frequent category.

The usual signs and symptoms are adequately discussed in standard texts and other sources. Repetition in this paper would serve no useful purpose.

Case reports

Case 1 (Hospital No. 353826)

K. L. G., a man, aged 59 years, was first admitted on February 10, 1948, with a swelling of the right upper lid. Visual acuity was 20/20, O.U., corrected. The left eye was completely normal. The right globe was normal but displaced down and in. Hertel readings were: O.D., 30 mm.; O.S., 14 mm. X-ray films showed a soft tissue density of the right superior orbit. Visual fields (3/330 and 1/1,100 white) were normal. Workup was otherwise normal or negative. Through a lateral superior lid approach two contiguous and encapsulated tumors were removed. The histopathology was that of a mixed tumor of the lacrimal gland. Three and a half years later on November 16, 1951, there was no evidence of recurrence.

He was readmitted on August 29, 1954, having noticed a recurrent proptosis of the right eye for eight months without pain. General physical examination was again negative. A bone survey was reported as negative. Visual acuity was: O.D., 20/50; O.S., 20/20, corrected. Hertel readings were: O.D., 20 mm.; O.S., 14 mm. A small, hard, nontender mass was felt in the region of the right lacrimal fossa. The left eye was completely normal. The right fundus showed a beginning senile macular degeneration. The previous sections upon review were thought to be more consistent with a neurofibrosarcoma. Biopsy tissue obtained through a superior lid approach yielded only normal lacrimal gland tissue.

Utilizing a classical Krönlein approach the orbit was exposed and the tumor mass was found to be adherent to the periorbita. Tissue obtained at this time appeared to be consistent with a recurrent mixed tumor. It was not disturbed further. However, two days later, after discussion with the patient, an exenteration was carried out and the orbit was lined with a split-thickness primary skin graft. The graft took very well and only had to be reinforced on the floor with a few pinch grafts.

This patient subsequently developed a left supraclavicular node which proved to be carcinoma of the thyroid. At the same time a small lytic lesion of the right third rib was seen on X-ray examination, which on review was faintly discernible in the previous films. This was biopsied and histologically proved to be tumor tissue similar to the exenterated specimen.

Pathology. All tissues were studied by many pathologists. The Armed Forces Institute of Pathology solicited the opinion of several outstanding

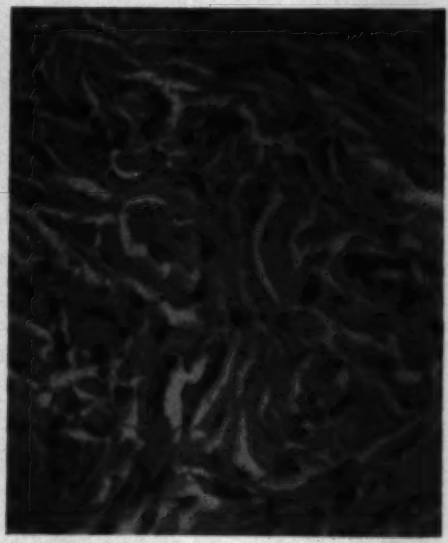

Fig. 1 (Beuerman and Tabor). Mixed tumor of lacrimal gland. Original specimen in 1948.

Fig. 2 (Beuerman and Tabor). Recurrent mixed tumor lacrimal gland removed in 1954.

pathologists, the majority of whom considered it a sarcoma, unclassified. Dr. Lorenz Zimmerman of the Armed Forces Institute of Pathology was of the opinion that the original and recurrent tumors in this case represented mixed tumor of lacrimal gland origin (fig. 1).

In Figure 1 we see an appearance of epithelial-like structures and a relative frequency of small capillaries. There are however areas where the condensation of round cells appears almost like epithelial cords. These cordlike structures are sparsely interspersed in a matrix of myxomatous looking connective tissue. In Figure 2 we see a relative increase in cellularity of the tissue with some round and some spindle looking cells with a decreased frequency of small capillary structures. The intervening connective tissue still appears myxomatous and no definite epithelial or cordlike structures are seen.

Diagnosis. Mixed tumor of the lacrimal gland (?).

Comment. This case probably represents a mixed tumor which was recurrent six years after the primary excision and had, in fact, already metastasized. It illustrates well the very useful Krönlein approach and its modifications and the false sense of security for both surgeon and patient when the tumor is treated by local excision. It is interesting that this patient had a concurrent and separate carcinoma of the thyroid with node involvement on the opposite side. It also demonstrates difficulties encountered sometimes in properly classifying recurrent neoplastic disease of the lacrimal gland.

CASE 2 (Hospital No. 465298)

R. R., a girl, aged five years, entered the hospital on October 12, 1952, because the parents had noted a loss of vision in the left eye for at least a month. General physical examination was within normal limits. Visual acuity was: O.D., 20/20 "E" chart; O.S., no light perception. The right eye was completely normal. Hertel readings were: O.D., 12 mm., O.S., 13 mm. The pupillary reactions were those of a blind left eye. The disc was elevated three diopters with slightly blurred margins and a dirty, grayish-white discoloration. There was increased orbital resistance on the left to global pressure. X-ray films revealed a markedly enlarged left optic foramen. Neurologic examination, including electroencephalogram, was otherwise noncontributory.

At craniotomy, using the transfrontal approach, the neurosurgeon found the left optic nerve to be quite enlarged from one mm. behind the globe to within three mm. of the chiasm. This whole segment was removed en masse. Sections revealed tumor infiltration in the distal cut end of the nerve, and the left eye was subsequently enucleated. Examination in April, 1956, revealed no evidence of recurrence.

Pathology. The histologic pathology revealed a marked diffuse proliferation of astrocytes, oligodendrocytes, and of arachnoid cells. The pia arachnoid cells projected into the thickened mass. The pro-

Fig. 3 (Beuerman and Tabor). Glioma of optic nerve.

liferating cells showed mild variation in size, shape, and staining reaction, and the nuclei were hyperchromatic. Frequent cytoid bodies were seen. There was an occasional small calcium deposit in the arachnoid (fig. 3).

Diagnosis. Glioma of the optic nerve.

Comment. This case represents the classical type of true glioma of the optic nerve found in the first decade of life. There was early monocular loss of vision, slight proptosis, papilledema, and enlargement of the optic foramen. The hyperplastic response of the overlying arachnoid to the glial tumor was also typical. No recurrence is anticipated. These tumors are benign or show a low-grade malignancy. The transfrontal approach was mandatory due to the extension of the tumor into the canalicular portion of the optic nerve. A Krönlein procedure would have been entirely inadequate. The surgical approach must be carefully planned and executed in each individual case of orbital tumor. The origin of this tumor cannot be stated with certainty; however, it involved the full orbital portion of the optic nerve and only part of the intracranial portion, therefore it is presumed to have been either orbital or canalicular in origin.

CASE 3 (Hospital No. 477665)

J. P., a man, aged 34 years, was admitted on November 4, 1953, complaining of a large swelling in the left upper lid which obscured vision. It had been present for 10 years with a slow, progressive enlargement. There was no history of trauma or inflammation.

General physical examination was normal. Visual acuity was 20/20, O.U. The right eye was normal throughout. The left globe was normal. The left upper lid was markedly enlarged by a thin-walled, translucent cystic mass which seemed to be attached laterally and had developed subconjunctivally into the upper lid. The cyst transilluminated well. Routine laboratory studies and blood Kahn, as well as X-ray studies of the chest and orbit, were normal or negative. Schirmer test indicated normal lacrimal fluid production. The cyst was removed from the region of the lacrimal gland through a conjunctival approach. The postoperative course was uneventful.

Pathology. The sections revealed a partially collapsed cystic structure with a well defined epithelial lining composed of cuboidal cells. Scattered about within the cyst were several nests of glandular tissue arranged in acinar fashion similar to normal lacrimal gland (fig. 4).

Diagnosis. Cyst of the lacrimal gland.

Comments. Cysts of the lacrimal gland, although not neoplastic, fulfill the requirements of an orbital tumor because they are posterior to the orbital septum. In Duke-Elder[3] one gains the impression that these cysts usually grow posteriorly into the orbit. In this case it extended anteriorly and developed subconjunctivally into the lid.

CASE 4 (Hospital No. 501620)

F. L. F., a man, aged 21 years, entered the hospital on October 2, 1954, complaining of a mass in

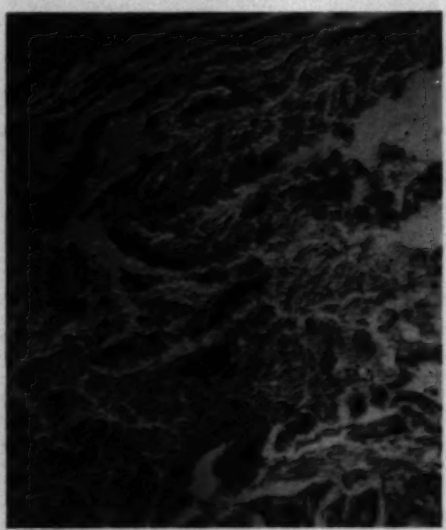

Fig. 4 (Beuerman and Tabor). Cyst of lacrimal gland, showing collapsed cyst walls with lacrimal gland tissue in the wall.

the medial aspect of the right upper orbit of six months' duration. General physical examination was within normal limits. Visual acuity was 20/20, O.U. The left eye was completely normal. The right eye was normal except for a slight lateral displacement without proptosis. Deep palpation revealed a smooth, nontender, rounded mass in the medial portion of the right orbit. It was semifluctuant. Routine laboratory studies and X-ray films of the skull, chest, optic foramina, and sinuses were normal or negative. Ear, nose, and throat examination revealed no sinus disease. Visual fields (3/330 and 1/1,000 white) were normal. Through a superior, medial transconjunctival incision a smooth tumor mass was found outside the muscle cone and attached by a broad fibrous band to the medial wall of the orbit. It was removed by sharp and blunt dissection. The postoperative course was uneventful.

Pathology. Sections revealed a cystic structure lined by squamous epithelium and surrounded by fibrous connective tissue. A fairly large number of sebaceous glands were present in the cyst wall. Large numbers of chronic inflammatory cells and small areas of old hemorrhage were also noted (fig. 5).

Diagnosis. Dermoid cyst.

Comment. This case was ideally treated by surgery, utilizing a transconjunctival approach. At surgery needle aspiration showed a very thick sebaceous type of material and confirmed the clinical impression of dermoid cyst. The broad, fibrous attachment to an adjacent osseous structure is quite characteristic of dermoid cysts. Aspiration biopsy is no substitute for adequate surgery in any orbital tumor. This procedure should not be used unless the surgeon is prepared to do whatever major surgical procedure is indicated at the same time.

Fig. 5 (Beuerman and Tabor). Dermoid cyst. Note the epithelial lining with adjacent sweat glands.

CASE 5 (Hospital No. 517167)

K. G. R., a 34-year-old woman, was admitted May 9, 1955, complaining of a gradually increasing mass in the left orbit for one year and double vision on upward gaze for six months. General physical examination was essentially within normal limits. Visual acuity was: O.D., 20/20; O.S., 20/20, corrected. The right eye was completely normal. The left fundus revealed mild blurring and hyperemia of the disc, but no hemorrhages, exudates, or measurable elevation. Hertel readings were: O.D., 12 mm.; O.S., 14 mm. Palpation of the left superior orbit revealed a deep tumor mass, the anterior projection of which was slightly irregular, nontender, and semifirm. The left eye was displaced downward and out and showed moderately limited supraduction.

Routine laboratory studies and X-ray films of the skull, optic foramina, chest, and sinuses were normal or negative. There was no evidence of sinus disease. Visual fields (3/330 and 1/1,000 white) were normal. There was a right hypertropia of about 30 prism diopters in upward gaze.

Utilizing a Benedict brow approach an encapsulated, slightly irregular tumor mass was found located between the periorbita and levator which extended to the apex of the orbit from the orbital septum. It was removed by blunt and sharp dissection. The postoperative course was uneventful. As soon as the postoperative reaction had subsided, ductions and versions were full and no diplopia could be elicited in the six cardinal directions with a red glass.

Pathology. Grossly, the cut section showed a yellowish mottled appearance with scattered irregular gray areas. It was fairly friable and of a fibrous consistency in the gray areas. Micropathology revealed a cellular tissue with palisading of spindle-shaped cells showing a tendency to form irregular whorled structures known as Verocay bodies. There was a thin envelope of fibrous tissue around the periphery suggestive of a capsule (fig. 6).

Diagnosis. Neurilemmoma, left orbit.

Comment. The Benedict brow approach was ideal for this case and gave fairly adequate exposure. The tumor, however, extended to the apex of the orbit and had to be removed primarily by blunt dissection. When the obstacle to binocular vision in upward gaze was removed, binocularity returned fairly promptly. The depressed position of the eye with a slightly sunken appearance of the upper lid persisted for six months.

CASE 6 (Hospital No. 532490)

G. T. C., a man, aged 21 years, entered the hospital on December 1, 1955. There was a history of trauma to the left eye six weeks previously with the slow development of a delayed proptosis. How-

Fig. 6 (Beuerman and Tabor). Neurilemmoma, left orbit. Note the palisading spindle cells.

ever, an identification photo two months before the trauma showed a definite increased prominence of the left eye.

General physical examination was within normal limits. Visual acuity was 20/20, O.U. The right eye and orbit were negative. The left eye was proptosed forward without displacement with some dilatation of the inferotemporal conjunctival vessels. Hertel readings were: O.D., 23 mm.; O.S., 32 mm. A firm, nontender mass could be felt on deep palpation through the left upper lid. Duction movements of the left eye were moderately but equally limited in all directions. Skull X-ray films, including optic foramina, revealed some osteoporosis of the left orbital roof.

The following examinations were normal or negative: Chest X-ray, EEG, blood count, urinalysis, blood Kahn, sinus films, arteriogram, and visual fields (3/330 and 1/1,000 white). There was no evidence of sinus disease.

A biopsy was taken from a tumor mass within the muscle cone through a transconjunctival incision. The histopathology revealed chronic granulation tissue with old hemorrhage. A trial of procaine penicillin, 300,000 units daily, for 10 days did not reduce the mass or the Hertel readings. X-ray therapy was considered, but was rejected by the therapist due to the uncertain nature of the tumor mass.

After an observation period of three months with the findings remaining the same, a surgical removal was effected utilizing the Benedict brow approach. A tumor mass 3.0 by 1.5 by 1.5 cm. was removed from the muscle cone. It extended from behind the globe to the apex of the orbit and was thinly encapsulated. It shelled out easily by blunt dissection. Hemorrhage was minimal.

When the postoperative reaction subsided, there was complete inability to elevate the left eye. The Hertel readings returned to 23 mm., O.U. After pontocainizing the conjunctiva the left eye could not be forcibly elevated with a forceps.

On August 14, 1956, five months after removal of the tumor, the left superior rectus was explored and found to be adherent to the globe from its insertion to the optic nerve. This was the location of the excised tumor mass. After freeing the adhesions as far posteriorly as possible the left superior rectus was resected five mm. and the left inferior rectus recessed four mm. Following this procedure the patient demonstrated binocular single vision in the entire lower fields of gaze and for about 25 degrees in upward gaze.

Pathology. Histopathology revealed hyalinized cicatricial tissue with some deposits of hemosiderin. There were collections of round cells, plasma cells, and lymphocytes but no true lymph follicles. A small number of thick-walled medium-sized blood vessels were seen in the fibrous stroma. There was a thin fibrous capsule (fig. 7).

Diagnosis. Pseudotumor.

Comment. This case presented primarily a palpable mass with marked proptosis. The latter was so prominent that after an adequate period of temporizing surgery was undertaken. The Benedict approach gave a barely adequate exposure, but no hemorrhage was encountered to explain subsequent events. The adhesions to the superior portion of the globe constituted an unusual complication. It is

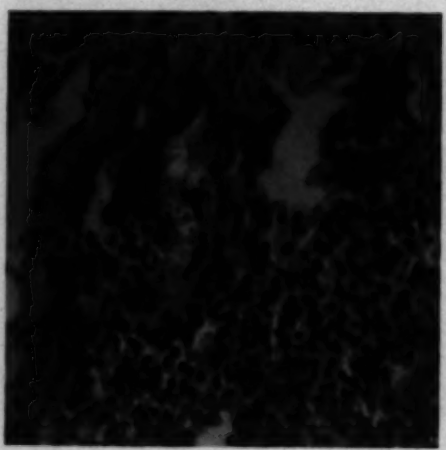

Fig. 7 (Beuerman and Tabor). Pseudotumor of left orbit.

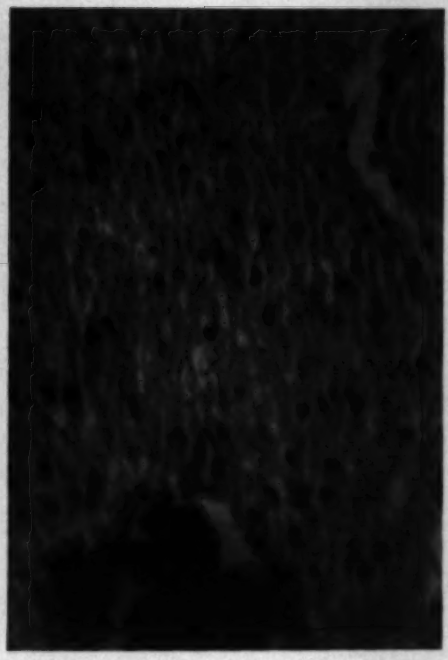

Fig. 8 (Beuerman and Tabor). Neurilemmoma, right orbit. There is a slight tendency toward palisading with a focus of calcification.

possible that the use of systemic cortisone or jelfilm might have minimized or prevented this complication. Pseudotumor is the cross every ophthalmologist must bear in the differential diagnosis of orbital tumors.

CASE 7 (Hospital No. 554854)

R. W., a man, aged 17 years, entered the hospital September 13, 1956. History revealed a fist blow to the right eye four years previously following which the eye became gradually more prominent without visual disturbance. General physical examination was essentially within normal limits. Visual acuity was 20/20, O.U. The left eye was completely normal. The right eye was normal except for a slight proptosis without displacement. Hertel readings were: O.D., 25 mm.; O.S., 18 mm.

The following examinations were negative or normal: X-ray films of skull, optic foramina, sinuses, chest, blood Kahn, routine laboratory studies, and visual fields (3/330 and 1/1,000 white).

A firm, nontender mass could be felt on deep palpation at the lower outer angle of the right orbit. The right orbit was explored using the Reese modification of the Krönlein approach and an elongated, smooth, firm, encapsulated tumor mass was removed from the infratemporal region of the orbit. It was outside the muscle cone. Postoperative course was uneventful. Hertel readings returned to 18 mm., O.U., and visual acuity remained 20/20, O.U.

Pathology. Grossly the specimen was thinly encapsulated with a slightly irregular surface. Areas of yellowish tissue were interspersed in a background of darker, grayish tissue. Histopathology revealed a moderately dense collagenous tissue with whorls and strands of spindle cells. There was a suggestion of palisading with numerous blood vessels and small foci of calcification. At the periphery of the tumor and in the extracapsular tissue were numerous small rounded structures resembling nerve bundles (fig. 8).

Diagnosis. Neurilemmoma, right orbit.

Comment. This case was ideal for the Reese modification of the Krönlein approach. Grossly neurilemmomas present a characteristic mottled yellowish and grayish appearance and have a slightly irregular feel when palpated. They are usually solitary, benign, and well encapsulated. Their removal presents no major problem when the proper surgical route is chosen. Neurilemmomas do not recur if completely excised.

SUMMARY AND CONCLUSIONS

Seven consecutive cases of primary tumor of the orbit which came to surgery during a five-year period have been presented in detail. Emphasis has been placed on the surgical approach.

Diagnosis by clinical methods is frequently impossible, the final answer being determined by the histopathology. The period of observation and study is usually long and extensive.

Primary orbital tumors are separated into four broad etiologic categories: inflammatory, vascular, endocrine, and neoplastic. Six of our cases were neoplastic and one inflammatory.

Ninety percent of all primary tumors of the orbit fall into the following pathologic groups. They are in order of frequency: hemangioma, dermoid cyst, lymphomatous tumors, pseudotumor, meningioma, glioma of the optic nerve, mixed tumor of the lacrimal gland, and peripheral nerve tumors. Five of these groups were represented in our series. The two cases of neurilemmoma and the absence of the commonest orbital tumor, hemangioma, make our series somewhat unusual. Our one case of cyst of the

lacrimal gland does not come under the eight common types.

The Benedict brow approach and the Reese modification of the Krönlein procedure are preferred when the tumor is confined to the posterior orbit. The transfrontal approach by a neurosurgeon is mandatory if it is anticipated that the tumor has extended into the optic canal or cranial cavity. Direct approach through the conjunctiva or skin of the eyelid may be utilized when the tumor is confined to the anterior orbit.

The surgeon should be prepared to perform a major surgical procedure with a view to complete excision of the tumor mass at the time of biopsy.

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A CLINICAL AND PATHOLOGIC STUDY OF EXFOLIATION OF THE LENS CAPSULE*

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This study was initiated after a discussion of Georgiana Dvorak-Theobald's paper on "Pseudoexfoliation of the lens capsule" at the American Ophthalmological Society meeting in 1953. At that time I showed some slides from two cases which were similar to hers, and I felt that the material found on the anterior capsule and in the posterior chamber was definitely an addition to the capsule and not a true exfoliation as such. I had difficulty in correlating the clinical picture, which appeared to be definitely an exfoliative process, with the pathologic picture, in which the material seemed to be built up from some material other than the capsule. At that time I felt this could be some product of deterioration from hemorrhage, which was present in one of my cases. Dr. Theobald[1] felt that this was not true, since none of the eyes she presented showed any evidence of hemorrhage. In her paper she did distinguish between the glassblower's type of exfoliation and the senile type which she called pseudoexfoliation. She felt that it was not a true exfoliative process, but a process of deposition as suggested by Busacca.[2] At that time I agreed with her. The present clinical and pathologic investigations have caused me to alter my opinion in regard to the nature and manner of the appearance of this exfoliative material. The evidence is still not absolutely clear for one or the other of these opinions, and perhaps there is evidence that both processes are occurring at the same time.

The material I would like to present is a clinical study of 62 patients with exfoliation of the lens capsule. Some of these patients have been followed for several years, and it is now possible to present some drawings and photographs of what I believe are the earliest changes in this syndrome. I hope that

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by studies of these and further photographs the entire development may be demonstrated. At present our knowledge is based on bits of evidence gleaned from different cases; no one case has been followed from the beginning to the final development. Exfoliation is a slow process, and the development of glaucoma, which I feel is definitely associated with this process, is an even slower process. Along with the clinical and photographic evidence, I would like to present some pathologic evidence based on a different technique for staining the lens capsule. This shows that the capsule is definitely made up of a cuticular and a zonular component, and that the cuticular component along with the germinal epithelium definitely does not enter into this particular syndrome. The zonular component, however, seems to have a very definite part to play, which will be shown later.

The clinical appearance of this condition is now generally recognized, and it is usually called senile exfoliation of the lens capsule to differentiate it from the so-called glassblower's type of exfoliation. The cases here reported are of the senile exfoliative type and show that there is a great deal of variety in the actual appearance of these cases, not only when they are first seen but also in the course of development. The length of time from the beginning to the end of one case has not yet been determined, but it is my impression that this is a matter of 10 to 20 years rather than three to five years. It is not a static condition, but one that changes continuously; the photographs show that this is for the most part a very slow change. Because the condition is actually changing, there is no "typical" picture. The earliest case, which begins in one eye and shows just the faintest changes in the capsule, seen only with a widely dilated pupil, is entirely different from the advanced case, which is bilateral and may show an advanced glaucoma in one eye or both eyes. I am still unable to present the complete picture, but I have been able to follow some unilateral cases from the onset until the syndrome has become fairly well established. The late picture is fairly characteristic and is well known. I shall, therefore, try to emphasize the earlier findings in this clinical discussion.

These 62 cases were found at a rate of one or two a year until 1947, when four cases were noted. Then four to six cases a year were found until 1954, when 11 cases appeared. In 1955 only six cases were discovered. In 1956 10 new cases were seen. This variation in the number of cases appears to be proportional to the interest and diligence in looking for this particular syndrome. It is not necessary to dilate the pupils to find the advanced cases. Many of these cases were discovered with the 20-diopter lens in the ophthalmoscope. The circular edge of the central disc is seen just inside the pupillary margin, as a fine dark irregular line. The early cases can be discovered only with dilated pupils.[5]

Analysis of these 62 cases shows that there were 31 males and 31 females. The average age was 71 years; for males 70 years, for females 72 years. The youngest patient was aged 46 years, the oldest 89 years. There were only 60 cases in which both eyes were present; 26 of these showed unilateral exfoliation (45 percent; the right eye in 15, the left eye in 11); 34 cases were bilateral (55 percent). The average age of unilateral cases was four years younger than that of the bilateral cases. In the group of 60 cases, 25 patients showed glaucoma

TABLE 1

NATIONAL BACKGROUNDS OF 62 PATIENTS

Scandinavian		14
Swedish	8	
Norwegian	3	
Dutch	2	
Danish	1	
Eastern Mediterranean		12
Syrian	5	
Greek	4	
Jewish	2	
Armenian	1	
Middle European		10
German	6	
Bohemian	2	
Polish	1	
Italian	1	
English, Irish, and Scotch		14
Mexican		1
Undetermined		11

(42 percent); 31 cases had cataracts and vision less than 20/100 (51 percent).

The nationality of these patients was for the most part available, and it showed the characteristic grouping; the disease apparently is more common among persons of Scandinavian[4] and eastern Mediterranean backgrounds.[5, 6]

It can be seen that Syrian, Armenian, and Greek people make up a larger group than would be expected from their population concentration in Omaha. Also the Swedish, Norwegian, Danish, and Dutch group appears to be larger than would be expected. These are the two groups referred to in the literature as showing this condition in a high ratio. There was a hereditary factor demonstrated in one father and son, suggesting that this is a hereditary condition but that it develops so late in life that it is difficult to establish this association. The father was 87 years of age, the son was 59. The son showed the condition in only one eye. This would never have been discovered if the pupil had not been dilated and the condition looked for because it had been found in the father. Twenty-five (42 percent) of the cases had glaucoma. These are analyzed as follows:

Nine unilateral cases, all with exfoliation in the glaucomatous eye (three had exfoliation in the glaucomatous eye only, and no eyes without exfoliation had glaucoma);

Sixteen bilateral cases, all with exfoliation in both eyes;

Nine cases blind from glaucoma in one eye with exfoliation in the other eye;

One case blind from glaucoma in one eye, no exfoliation or glaucoma in other eye.

This would indicate that glaucoma is found in cases with exfoliation more frequently than in the average run of patients. Other series of cases of exfoliation show various percentages, depending on the source of the material. If the cases come from the Glaucoma Clinic, and the pupils were dilated, the number is high. Hörven shows 93 percent;[4] Vogt 75 percent;[7] Rehsteiner 70 percent,[8] also 78 published cases, 64 percent with glaucoma; Irvine 50 to 75 percent; Trantas 33 percent;[5] Garrow 16 percent;[9] Busacca 76 percent (Glaucoma Clinic); Sobhy Bey 54 percent;[10] Gradle and Sugar 72 percent.[6] In spite of this, others think that exfoliation is not the cause of glaucoma.[11–16] Grzedzielski[17] was doubtful.

I have felt that the exfoliative syndrome also has something to do with the production of cataracts; 31 (51 percent) of the cases had cataracts with vision 20/100 or less. These break down in the following manner:

Of 16 unilateral cases with cataracts, nine were associated with exfoliation in both eyes, seven were associated with exfoliation in only the cataractous eye.

Of 15 bilateral cases, all except one had exfoliation. One without exfoliation had a cataract.

From this it would seem that the presence of a unilateral cataract in an older person may indicate the presence of exfoliation of the capsule. When a cataract is present the exfoliation may be very difficult to see. Other series of cases show similar association with cataract: Trantas 71 percent, Gradle and Sugar 38 percent, Busacca 24 percent.

In attempting to evaluate the treatment of the glaucoma in these cases, I found that medical treatment was ineffective. All the cases were tried on Pilocarpine, many for several years before surgery.

One case was controlled with Pilocarpine (one percent) for three years.

Fourteen cases were observed for the following periods with no development of glaucoma:

Cases	Years
1	8
1	6
2	5
2	4
2	3
4	2
1	1
1	6 (mo.)

One case developed glaucoma after a period of 10 years.

This shows that the development of glaucoma takes many years.

There were 13 glaucoma operations performed, two of these by my father, who probably did not recognize the exfoliation.

TABLE 2

ANALYSIS OF 13 GLAUCOMA OPERATIONS

Type of Operation	Number Performed	Number of Years of Successful Follow Up
Curran	1	18
Iridotasis	1	24
Trephine	2	2
Sclerectomy	2	12
Sclerectomy	1	6
Sclerectomy	1	3
Sclerectomy	1	2

One sclerectomy was successful for at least two months, and one failed; two attempts at cyclodialysis also failed.

These results do not seem much different from the results with ordinary glaucoma.

There were 22 lens extractions in this series of cases; 19 were done principally to cure the glaucoma, and three were for cataracts. All but one had some lens opacity. The results of the extractions for glaucoma were as follows:

Cases		Years Successful
6	at least	3
2	at least	2
6	at least	1
3	less than	1

Two extractions failed to reduce tension.

Thus it would seem that the glaucoma associated with exfoliation may be satisfactorily treated and controlled in most cases by either a cataract extraction or a filtering operation. It is my opinion that if the lens shows beginning opacities, a lens extraction would be the operation of choice. There were no surgical complications peculiar to the syndrome in any of these operations. The lens dislocated easily without rupture of the capsule. There were no vitreous losses or signs of fluid vitreous, as had been suggested by Gradle and Sugar.

In the group of 62 cases there were three in which there was a spontaneous dislocation of the lens. This would indicate that the zonule in these patients is more friable than normal. This has been suggested by Gradle and Sugar, also by Dr. Irvine. Dr. Sunde in his recent anatomic and pathologic studies indicated that the zonule was not usually inelastic or friable.

There were six cases in which a pigment cloud was seen in the anterior chamber following dilation of the pupil. This has been pointed out by many writers on this subject, and in these cases it would seem to mean that the iris is applied directly to the lens capsule, and when the iris is dilated there is a tearing force which breaks the epithelium away from the posterior surface of the iris. The cloud in the anterior chamber is transient but definite. The pigment tends to drop out on the exfoliated material on the capsule, the surface of the iris, and into the lower anterior chamber angle. This produces the deeply pigmented trabecula found on gonioscopic examination of most cases of exfoliation. This fine pigment may also be seen on the surface of light-colored irises and may be a definite indication that exfoliation is present. Under normal conditions the pupil is never as widely dilated as it is under the influence of drugs. We are, therefore, in using these drugs, setting up an artificial situation which may influence the exfoliation for better or for worse. I am sure that it produces more extensive peeling of the exfoliated material. It is my impression at present that this is a good thing in the early cases, but it may be a bad thing in more advanced cases.

In the early cases it may be possible to scrape off this exfoliated material and pigment into a trabecula which is more capable of handling it. This may prolong the useful drainage of that angle and postpone the development of glaucoma. In the older cases, however, where this exfoliated material is dumped into the chamber in large quantities, it is theoretically possible to hasten the development of glaucoma by adding an insult to an already handicapped

trabecula. In most cases the tension was definitely lower shortly after dilating the pupil with euphthalmine and Neosynephrine (10 percent). In no case did the tension rise with dilatation. Neosynephrine was tried as a therapeutic agent in one case, but it did not continue to hold the tension down.

In the last two years I have been able to photograph 26 of these cases of exfoliation. This allows a more detailed study and comparison of one case with another. These photographs were taken with the Zeiss photographic attachment to the slitlamp, twice magnified, lens opening at f.22 at 1/30 of a second, Tri-X film. A gonioscopic contact glass which increases the magnification about eight times was also used to gain better detail. In analyzing these 26 sets of photographs, which comprise several hundred individual pictures, I was surprised to find that there appeared to be two types of exfoliation. The exact relationship of these two types is not yet quite clear, but they are definite enough to be classified. The first type is the more common one, and it is characterized by a central disc which is continuous, at least in the early stages, with the peripheral frosty zone. This I have called the "wide band" type.

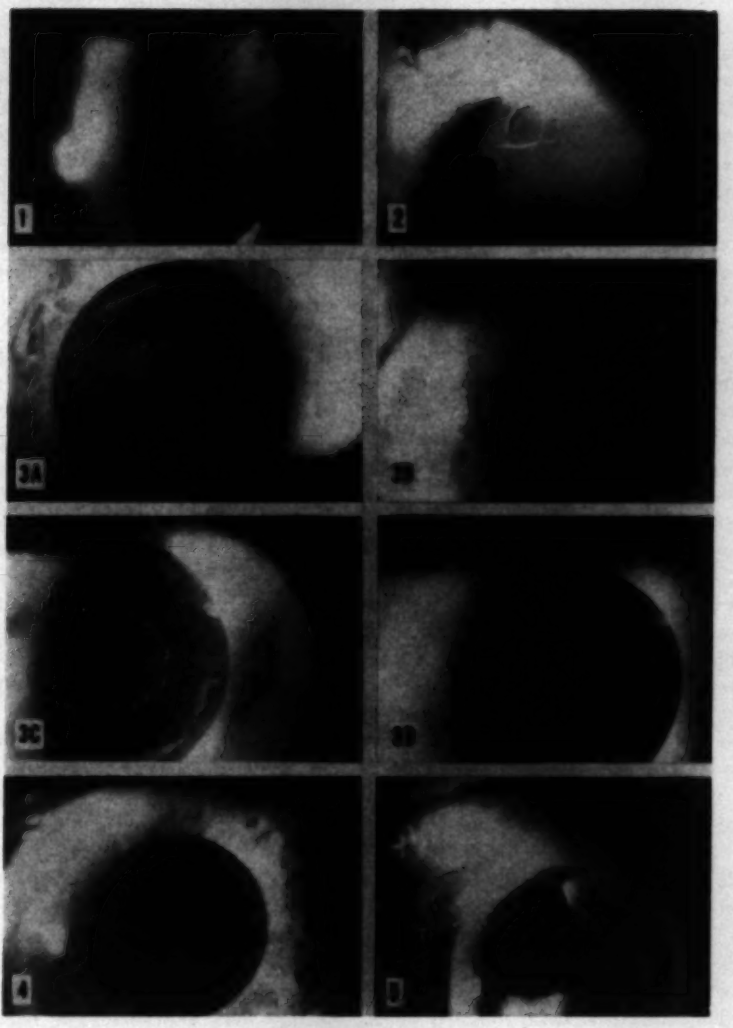
Figure 1 is a very early example with no peeling, no flakes. It shows a radial pattern that is probably related to the folds on the posterior surface of the iris. The ends of the frosty zone reach the central disc.

As the condition develops the peripheral bridges become narrower, the holes in the intermediate zone become larger, and the band becomes narrower. This leads to a condition where the central disc is quite prominent, with curled-in edges; the peripheral zone has curled-out edges.

Figure 2 shows the secondary frosty zone developing. At a later stage there are flakes of exfoliated material on the central disc and also on the pupillary margin of the iris. At a still later stage the bridges are nearly all gone and the wide band has become a narrow one. Figure 3 shows the progress of this case: in Figure 3A may be seen a flake peeling from the periphery and flakes on the central disc; 3C shows the large flake on the iris margin and the narrow, irregular peripheral zone. Figures 3B and 3D were taken 10 months later. The deposit on the central disc has not changed, nor has the secondary frostiness. The flake on the iris margin at the 2-o'clock position has not changed. The peripheral zone at 3-o'clock position is only slightly narrower.

Among the 13 unilateral cases, this wide band type was present in its early form in six. There was no dandruff and no curled edge, but the peripheral frosty zone was wide and the tension was low and equal in both eyes. A later stage of this wide band type was found in four cases. These all showed considerably higher tension in the eye with the exfoliation; 27 mm. Hg in three eyes, 32 in one.

There were three cases in which the peripheral zone of frostiness was quite narrow, and it seems that this zone had never been wide. The central disc in the case illustrated in Figure 4 is barely visible; it is not outlined by any curling of the edges, and there is no exfoliated material precipitated on the disc itself. Two cases were like this one. There was slight deposit on the central disc, and there was a suggestion of peeling in the central disc in the other case. There was no dandruff on the iris margin. The narrow zone was for the most part a solid sheet with an occasional hole. The edges definitely curl backward toward the equator of the lens. This I have called the "narrow band" type of exfoliation. In these cases the tension was also equal in both eyes, and it was low. Since these photographs are all less than two years old, it has been impossible to follow any one of these cases long enough to make definite conclusions. It seems to me, however, that these unilateral cases fall into two separate groups, with two stages in the first wide band type. In the second stage of the wide band type, where the central disc had become well defined and there was definite



Figs. 1 to 5 (Gifford). (1) O.S., unilateral early wide band type. Tension 22 mm. Hg, O.U. (Schiøtz). (2) O.D., unilateral wide band type. Tension 17 mm. Hg, O.U. (Schiøtz). (3) O.D., unilateral wide band type becoming narrow, only one bridge remaining. Tension: O.D., 27 mm. Hg; O.S., 20 (Schiøtz). (A) October, 1955. (B) November, 1956. (C) October, 1955. (D) November, 1956. (4) O.S., unilateral narrow band type. Tension 19 mm. Hg O.U. (Schiøtz). (5) Fine deposits on hyaloid in area of coloboma 18 months after operation.

dandruff on the iris margin, the tension was always higher in the eye with the exfoliation. These are the cases that I believe will develop glaucoma in the near future. The cases showing the narrow band type have not yet developed any rise in intraocular pressure.

There were only six of the 12 bilateral cases in which both lenses were present. The photographs of these showed five cases of

the wide band type; three of these patients had unilateral glaucoma. The other six bilateral cases had intracapsular cataract extractions. There was usually some exfoliative material left on the hyaloid and the iris margin. In five of these cases there has been no increase visible in from one to three years of observation. Figure 5, however, shows material deposited 18 months after a cataract operation in April, 1954. There was no exfoliated material on this hyaloid from October of 1954 until November of 1955. Since that date, dusting on the margin of the hyaloid has increased and the tension has risen from 20 to 32 mm. Hg. Exfoliated material has appeared in the region of the iris coloboma. This was thought by Dr. Sunde to be impossible, and it was not found in any of his cases in which the lens was present. He felt that the presence of the iris was necessary for the formation of exfoliative material on the lens capsule. Apparently in this case it was not necessary for its development on the hyaloid following lens extraction. It is interesting to note that of these six bilateral cases, three had one eye that was blind from glaucoma. In one case the glaucoma and cataracts were bilateral, and in another the cataract and exfoliation were unilateral with no exfoliation in the opposite eye.

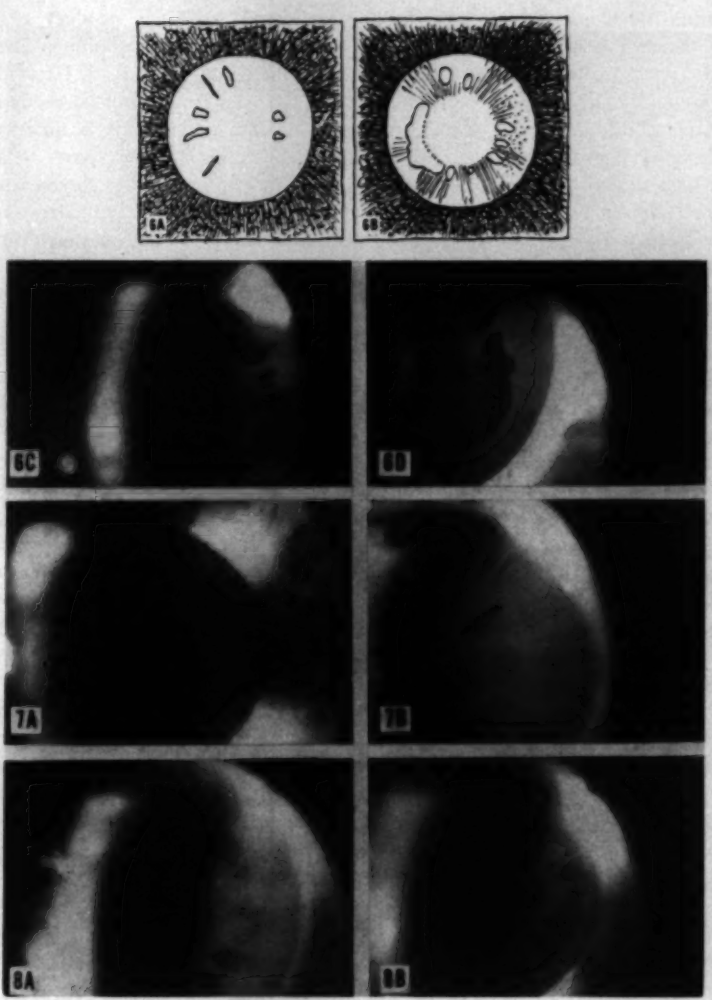
The development of the wide band type is shown in Figure 6. This is a unilateral case that has been followed for five years. The drawings and photographs demonstrate the slow progress. In 1951 there were holes only in the wide frosty peripheral zone. By 1953 these holes were becoming confluent. In 1955 there was only one wide bridge remaining, that with one hole in it. By 1957 this last bridge had nearly disappeared. Flakes of debris were piled up on the central disc with still very little curling of the edge. There has been no evidence of any secondary material forming. This eye has shown no appreciable tendency to increased pressure. The other eye shows no signs of beginning exfoliation.

Figures 7 and 8 show two early unilateral cases demonstrating the very slow enlargement of the holes in the frosty zone. Some areas show no change at all in one year. These clear areas seem to enlarge without producing a curled edge. At a later stage a definite curled edge develops.

Figure 9 demonstrates the hereditary nature of this condition.

Figure 10 shows a unilateral narrow band type of exfoliation which has shown a rapid change. In six months the peripheral zone has been reduced to one-half its former extent. The material has simply disappeared. There is no debris on the central disc. There has been no increase in the intraocular pressure. I have not seen this rapid and marked change in any of the wide band types.

From the clinical and photographic evidence, in the wide band type, the exfoliated material seems to arise on the capsule as a frosty granular sheet extending to the central disc. This becomes more granular with time, and it is definitely rubbed off by the action of the iris. Some material sticks to the iris margin and on the central disc, some is washed into the chamber angle. In some cases there is evidence of a secondary zone of frosty material occurring underneath the primary one which has peeled off. I have never seen this develop, and I was not able to find any cases where this zone had become frosty when it was clear at a previous examination. The secondary frostiness appears to develop beneath a peeled-off flake, but it is never so extensive as the original. It never extends to the central disc. The peeling process is a very slow one. The flakes apparently are not soluble in the aqueous, but I have seen the central disc disappear following a glaucoma operation. Glaucoma appears to develop slowly and only after there has been extensive exfoliation and the wide band has been brushed off and converted to a narrow band with the loss of considerable anterior capsular material. The fate of all this material is not known for certain. Some of it is found on the posterior cornea and in the chamber angle, although not in large



Figs. 6 to 8 (Gifford). (6) Unilateral wide band type. (A) October, 1951, tension 17 mm. Hg. (B) November, 1953; (C) December, 1955. (D) July, 1956, tension 19 mm. Hg. (7) Unilateral early wide band type. (A) November, 1955, tension 14 mm. Hg, O.U. (B) July, 1956, tension 20 mm. Hg, O.U. (8) Unilateral early wide band type. (A) September, 1955, tension 17 mm. Hg, O.U. (B) January, 1957.

amounts. Clinically the central disc is a definite structure and appears in this wide type of exfoliation to be definitely outlined by breaking away of the peripheral zone at its margin.

In the second type of exfoliation, where the peripheral zone is narrow, the central disc appears as a homogeneous, optically more opaque, gray area which occasionally has flakes of exfoliated material on its surface or outlining its margin. In this narrow band type there was one example of rapid deterioration of the peripheral frosty zone with almost complete disappearance over a wide area. These cases have so far shown no tendency to develop glaucoma. In both types

the condition develops in one eye first, and in the other eye many years later. By the time the cases are bilateral the incidence of glaucoma and cataract has increased. In late stages glaucoma is usually present in at least one eye. When cataracts are present there may be a similar situation, a unilateral cataract with bilateral exfoliation. In spite of the recent work by Sunde, it seems to me that the mass of clinical evidence indicates that this exfoliation syndrome is definitely associated with chronic simple glaucoma. I believe we would find glaucoma developing in most cases if the patients were to live long enough and their progress could be followed for 20 or 30 years. Clinically, some of this material of exfoliation comes from the surface of the capsule and is rubbed off by the action of the iris. The position of the iris in relation to the lens capsule may have something to do with the development of the wide and narrow band types.

Pathologically there are two different opinions. Vogt and his followers believe that this material is definitely a deterioration product of the zonular lamella of the lens capsule, whereas Busacca and his followers, and more recently Sunde, feel that it is definitely a deposition from the aqueous. The work of Sunde has cleared the air to a great extent in showing that the "deposits of Busacca" are definitely the same as the material of exfoliation seen by Vogt in his clinical cases. The gross pathology has been well shown by Sunde. He feels that the absence of any microscopic change in the lens capsule would indicate that this must be a deposit on the capsule. He was unable to demonstrate any histologic changes in the capsule such as Vogt showed in his early cases. He did not use any special stains except the Hotchkiss-McMannus, which does not satisfactorily differentiate the zonular from the cuticular lamella.

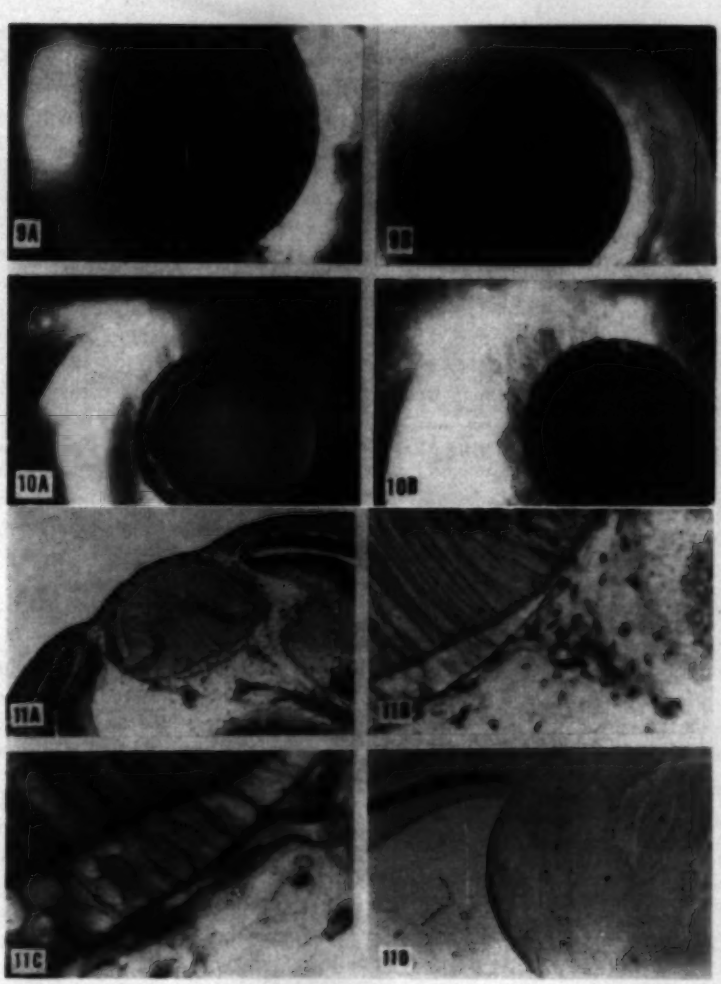
In order to understand the pathology of this region I have attempted to clarify the embryology and anatomy in my own mind. Embryologically the capsule is in general considered to be a product of the lens epithelium.[18] After examining several small embryos in the laboratory, I found evidence that the posterior capsule is really laid down at an earlier period than the anterior capsule. This posterior capsule seems to arise as a direct derivative of the mesodermal tissues forming the hyaloid vascular network. A 22-mm. and a 17-mm. specimen each showed definitely the formation of the capsule on the posterior surface of the lens where there is no special germinal epithelium. The anterior surface showed no evidence of this type of membrane.

In Figure 11, A-C, the 17-mm. embryo is illustrated. In the low-power view (A) the lens vesicle is still present and there is no evidence of a capsule on the anterior surface. In the high-power view of the posterior equatorial region (B) a faint line of capsule is seen associated with an embryonic hyaloid vascular network. In the oil immersion of the same area (C) the membrane is quite distinct.

There is a well-defined capsule surrounding the lens in the 45-mm. specimen (D), and there is still no zonule. It is my opinion that at least the outer layer of the capsule is mesodermal in nature and may be said to arise from the embryonic hyaloid vascular network.

Kirby has spoken of a dual origin of the zonule, and he may well be correct. In his discussion of Theobald's paper at the American Ophthalmological Society in 1953, he expressed the opinion that

> the pericapsular membrane which is on the anterior surface of the lens and the viscous material which invests these zonular fibers are of a similar origin and similar nature. I believe that Dr. Theobald has added further information which will lend credence to my postulate that the zonule is of two origins, first the zonular fibers that developed as extensions of the protoplasmic processes, which develop when the optical vesicle touches the surface ectoderm. When the optical vesicle invaginates and the lens recedes into the optic cup, the fibrillar connections are stretched out. At the time of the formation of the tertiary vitreous the viscous material may be added. Thus we may say there is a dual origin for the zonule. In the adult position the fibers



Figs. 9 to 11 (Gifford). Hereditary exfoliation. (9) (A) Son, age 59 years; unilateral early wide band type, tension 22 mm. Hg. (B) Father, age 87 years; late wide band type, tension 32 mm. Hg, other eye tension 83 mm. Hg. (10) Unilateral narrow band type. (A) August, 1956, tension 19 mm. Hg, O.U. (B) March, 1957, tension 19 mm. Hg, O.U. (11) Development of lens capsule in embryos. (A) 17-mm. embryo, low power. (B) 17-mm. embryo, posterior equatorial region, high power. (C) Oil immersion of same area. (D) 45-mm embryo, low power.

measure about seven mm. I believe in some cases there is a degeneration of the viscous material of the pericapsular membrane and of the material which invests the zonular fibers.

This expression of Kirby's comes fairly close to the expression of several other students of this condition. Irvine, Gradle, and others feel that it is the zonule and the zonular lamella of the capsule which are involved in this exfoliative process. Busacca clarified some of the confusion by pointing out that the pericapsular membrane could be stained with silver and that the zonule and this pericapsular membrane are probably the same material which extended completely

around the lens. Most writers have not been careful to separate these two structural portions of the lens capsule, the capsule being merely referred to as one large anatomic structure. It occurred to me that if special stains could be found that would separate these two anatomically and possibly embryologically different structures this problem could be clarified. McCulloch,[19] in his recent work on the zonule, states that the opinion today is in favor of the zonule being ectodermal in origin, quoting Mann, Vail, and Mertz; but he shows also a good deal of evidence that the zonule may well be mesodermal, coming from the vascular part of the primary vitreous, quoting Lenz, Houfek, Braily, and Cirincioni, who feel that there is a double origin.

The anatomy of the zonule is even more confused, and there is still no definite opinion as to the exact structural composition of the zonule and the zonular lamella of the lens capsule. McCulloch[19] used the Hotchkiss method with Gommori's chromic hematoxylin to stain the zonular fibers. In both stains it appears dark blue, almost black with Gommori's stain, and is sharply separated from the paler cuticular part of the lens capsule.

With this stain the zonular lamella can be traced all around the lens and is thickest at the anterior and posterior coronal lines of insertion of the zonule, but is thinner at the equator of the lens. It can be traced across the anterior part of the lens where it is quite thin. It also can be traced across the posterior pole of the lens, although here it shrinks to a faint dark blue line. Although it may be possible to show fibers passing between the zonular lamella and becoming lost in it, in the anterior and posterior coronal lines of insertion the fibers run parallel to the lamella and just fuse with it. At the equator the zonular fibers break into a brush of fibrils which are lost in it.

In my attempt to separate these two structures histologically I found that the Wilder silver stain and the phosphotungstic acid stain also show this zonular lamella quite well. Even better, however, was the stain of Reinhart–Abul-Haj.[20] This particular stain was developed to separate basement membrane from reticulin. Reticulin contains carbohydrate which can be demonstrated by various oxidative methods of staining. Reinhart's technique is based on one of Hale (1946), which is dependent on the affinity of acid mucopolysaccharides for colloidal iron and their subsequent delineation by the Prussian blue reaction with ferrocyanide. In the Reinhart–Abul-Haj (1951) method, this includes appropriate counterstaining with cochineal and fuchsin. The ground substance stains blue. The basement membrane stains yellow to orange, collagen fibers red. This is the reaction of the stain used in these present studies. Further histochemical stains designed especially for reticulin, such as the combination of Gommori and the Hotchkiss-McMannus suggested by Lillie,[21] might show the exfoliated material even clearer than the Reinhart stain, since the Reinhart stain is chiefly designed to bring out the basement membrane.

It seemed to me from these stains that the zonule is a reticulinlike substance and that the cuticular part of the lens capsule is a true basement membrane. The cuticular part of the capsule stains bright orange-red, the zonular part being dark, either green, black, or blue.

The pathologic material I would like to present consists of sections from three eyes with exfoliation stained by Reinhart's method and from six lenses removed at cataract operations from eyes showing exfoliation clinically. These lenses were compared with a group of cataractous lenses, without exfoliation, from people in approximately the same age group. Several whole eyes with normal lenses were used for comparison.

The three whole eyes, which were enucleated for glaucoma, and which showed exfoliated material on the capsule and structures of the posterior chamber, all showed the cuticular part of the capsule to be normal. The exfoliated material was lying on the surface, but it appeared to be intimately associated with the zonular elements of the capsule. Figure 12 (Reinhart stain) shows

the typical findings in an eye enucleated for glaucoma.

In this case there was some carry-over into the zonular fibers, in places, of the red-orange basement membranelike staining. This would indicate the dual nature of the zonule. In all of the cases the exfoliated material was characteristic of the "deposits of Busacca" and stained dark blue, as did the rest of the zonule and the zonular lamella. In these enucleated eyes no definite thickening of the zonular lamella could actually be seen. The exfoliated material seems to be taking the place of the zonular lamella and growing from it in brushlike or treelike projections. The bulk of this material is several times greater than the bulk of the normal zonule. It may be simply fluffed up, or there may be some proliferation.

The normal relationships of the zonular lamella to the cuticular lamella are shown in Figure 13 (Reinhart stain). It shows well how thick the zonular lamella is at the equator of the lens. The zonular lamella extends over the anterior and posterior parts of the capsule where it is shown as a relatively thin, narrow line.

Figure 14 shows the appearance of the zonular lamella in cataractous lenses removed surgically.

These are two separate cases, stained by Reinhart's technique, and they demonstrate that the zonular lamella in these cases is a rather thin structure; only one case showed any tendency to thickening. This occurred toward the center of the lens capsule, taking on some of the characteristics seen in the cases with exfoliation. This may be an artefact or simply a senile change. It was seen in only two of the normal specimens.

There were six lenses showing exfoliation of the lens capsule removed surgically and stained variously to differentiate the cuticular from the zonular lamella. Two of these lenses are from the same patient. Both show a definite thickening of the lens capsule two or three times its normal thickness. Figure 15 shows one of these lenses.

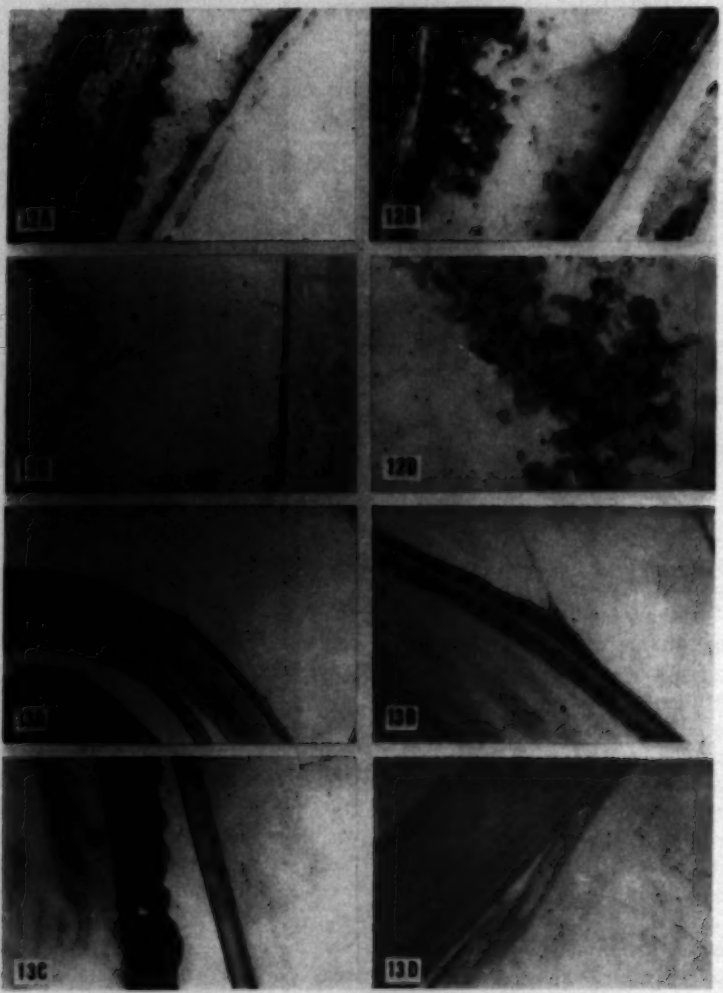
The extra thickness takes the characteristic stain with Reinhart and stains dark with Wilder's silver impregnation. The cuticular lamella retains its normal thickness. The zonular lamella has small cystic spaces which are exactly like those shown in Vogt's pictures.[21] The exfoliated material was not definitely associated with this cystic development, however. The other four specimens show less pronounced thickening of the zonular lamella. In one, the exfoliated material was covered with pigment which fits tightly to it and surrounds the exfoliated material to a large extent.

The exfoliated material stains dark with Reinhart's stain and appears to be continuous with the zonular lamella at the equatorial region. Examination of this material with the phase microscope was rather disappointing; the material appeared to have intimate contact with the zonule fibers. Figure 16 shows the dark and light phases. The tufts of exfoliated material stand on a definite membrane and have definite cores and branches. Examples of the dark and light phase are shown in the pictures.

An attempt was made to determine whether the germinal epithelium was involved in this process by making flat preparations of the lens capsule. This is shown in Figure 17. This shows quite definitely that the pattern of the germinal epithelium was not disturbed where the exfoliated material was peeling back from the capsule, and that the germinal epithelium was unchanged in the region of exfoliation.

Summing up this rather meager pathologic evidence, it seems to me that one thing is shown quite clearly: the germinal epithelium and the cuticular portion of the lens capsule play no part in this exfoliative syndrome. This explains why it is possible to remove these lenses in capsule and why there are no spontaneous ruptures of the lens capsule reported clinically. There is some evidence in a few of these cases that the capsule is definitely thicker than normal. This was also reported by Rehsteiner.[8] This thickening of

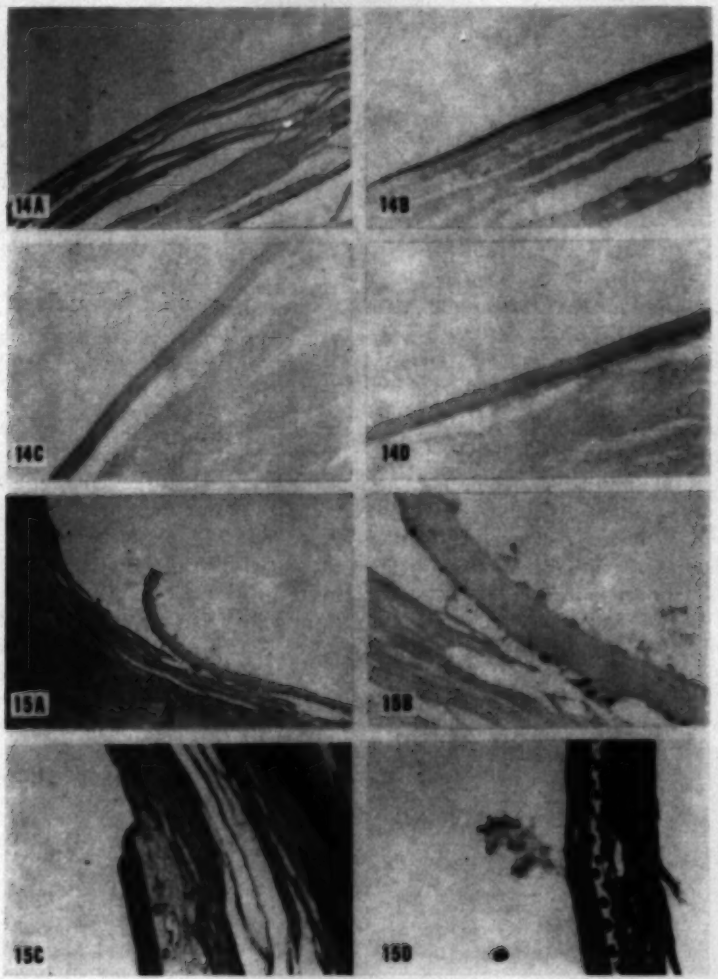
the capsule is chiefly of the zonular lamella and not of the cuticular portion. This zonular part appears to have thickened developed spaces, and to be eroding in some sections. This thickened layer could not be traced directly into the exfoliated deposits. The deposits, however, seem to grow out of and to be intimately associated with the zonule.



Figs. 12 and 13 (Gifford). (12) Exfoliation of lens capsule. (A) Reinhart stain, low power; cuticular layer of capsule is bright orange, exfoliated material dark to light blue. (B) Reinhart stain, high power; material on capsule and posterior iris. (C) Reinhart stain, low power; mass of material on zonular fiber and anterior surface of hyaloid, red blood cells in vitreous to right. (D) Reinhart stain, high power; some orange stain of zonular fibers with blue-staining exfoliative material on them. (13) Normal lens. (A) Reinhart stain, low power; zonule and zonular lamella are greenish, cuticular lamella orange. (B) Reinhart stain, high power; attachment of zonule posterior. (C) Reinhart stain, high power; zonular layer becomes thin near center of lens. (D) Reinhart stain, high power; zonular layer is thin surrounding posterior capsule; hyaloid fibers to right.

Histochemically the zonule appears to be similar to reticulin, and is not a basement membrane.

Just why the material can be rubbed off from the capsule and the zonule easily, and why it sticks so tenaciously to the iris and ciliary process, is not clear. Sunde in his work brings out this difference very plainly,



Figs. 14 and 15 (Gifford). (14) Cataractous lens without exfoliation. (A) Reinhart stain, low power; thin zonular lamella becomes thicker centrally to right. (B) Reinhart stain, high power; zonular layer slightly thicker. (C) Reinhart stain, high power; zonular layer thickens toward equator. (D) Reinhart stain, high power; lamellar layer slightly thicker and darker toward center. (15) Exfoliation of lens capsule (surgical specimen). (A) Hematoxylin-eosin, low power; no differentiation of central and zonular lamellae. (B) Hematoxylin-eosin, high power; capsule thickened with exfoliative material on surface. (C) Reinhart stain, high power; thickened, outer two thirds (zonular part) is green; inner cuticular part is red, not thickened; vacuoles separate layers. (D) Wilder stain, high power; zonular layer is thick and black, cuticular layer red; small vacuoles; exfoliative material on zonular layer is brownish.

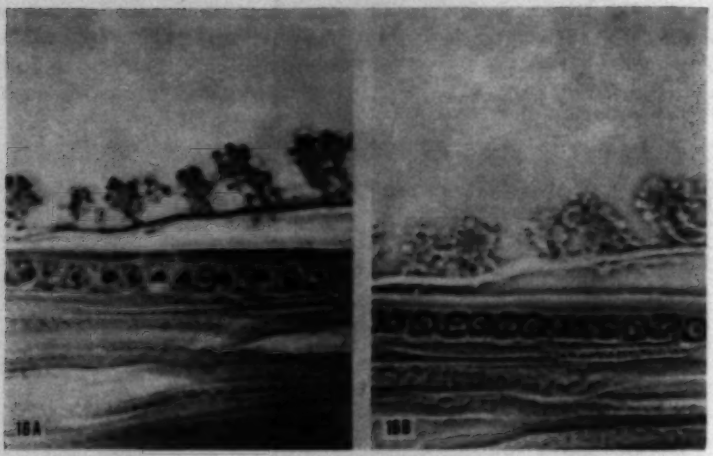


Fig. 16 (Gifford). Exfoliation of lens capsule (surgical specimen). (A) Microscope (dark phase) shows central core of treelike structure coming from zonular fiber. (B) Light phase shows opposite contrast.

but he has no real explanation for it. He feels that in both cases the material arises *in loco*, that is to say, it has not been transported from any distant point.

Anatomically, there is definitely a limiting membrane on the internal surface of the ciliary body which Salzmann[22] feels covers the ciliary epithelium and from which the zonular fibers can be seen to arise. This he called the internal limitating membrane which is carried over onto the posterior surface of the iris on the pigment epithelium for some distance. McCulloch, on the other hand, believes that the limiting membrane is not present on the surface of the ciliary processes. It is partly because of this that McCulloch places the origin of the zonular fibers in the valleys and feels that none of them come from the ciliary processes themselves. Salzmann also had this conception of the origin and source of the zonular fibers, but he feels that there is a definite limiting

Fig. 17 (Gifford). Flat preparation of lens capsule (Hematoxylin-eosin) showing normal pattern of germinal epithelium.

membrane across the ciliary processes. If this membrane is not present on the ciliary processes, it could not produce the exfoliating material which is found on these processes. If, however, there is a reticulinlike membrane over the surface of the ciliary process and the posterior surface of the iris, these deposits could arise from this membrane. From what I can tell with my Reinhart stains of this region and in examining these tissues with ultraviolet light, it seems to me that, at least in some eyes, especially those of older people, the internal limiting membrane is present over the ciliary processes and that it does extend on to the posterior surface of the iris.

In examining these specimens with ultraviolet light, the cuticular membrane of the capsule shows extremely bright fluorescence when hematoxylin and eosin stains are used. The zonule has a slightly less fluorescent appearance and, in some cases, is perhaps slightly more orange. The internal limiting membrane of the cilary body and posterior iris could be seen very well in some eyes. In others it was not seen at all. The exfoliated material appears to be physically similar to the zonule, fluorescing slightly less brightly than the cuticular lamella and having a slightly more orange appearance. With Hotchkiss-McMannus stains in the ultraviolet light the cuticular membrane appeared bright red with only a small amount of fluorescence. The zonule was considerably paler and was not well differentiated. The exfoliated material was very pale, barely visible. With the Reinhart stain, the cuticular membrane appeared bright red with considerable fluorescence. The zonule, however, was dark except where it seemed to contain a central core of cuticular material. The exfoliated material was also dark and showed up quite plainly in contrast with the red fluorescent cuticular part of the capsule. This would indicate some chemical difference between the zonule and the cuticular membrane.

It seems to me that there is evidence for a reticulinlike membrane which covers the anterior and posterior surfaces of the lens capsule and extends out over the zonular fibers. This reticulinlike substance extends over the surface of the ciliary processes, is thicker in valleys, and also extends on to the posterior surface of the iris in at least some places. The exfoliated material arises only in these places where the reticulin membrane is found anatomically. It is in these places that it arises in its characteristic treelike fashion, with the central trunk and bushy tops forming rows and ridges similar to hedges. No one yet has been able to explain why it takes this particular configuration. It seems to me that it must arise as an outgrowth from the zonular lamella and through some process of budding and growth develop these branchlike tufts on the surface. If this were a deposit from the aqueous, it would fill in all the valleys and leave a smooth surface without any ridges, tufts, or bumps. The development must be more like the coral in the ocean or crystals in a supersaturated chemical solution. Just how this occurs with this exfoliative material it is impossible to say at this time.

At present my feeling is that the exfoliation of the lens capsule is a true degenerative disease of the zonule and the zonular lamella of the lens capsule. The exfoliative material is definitely rubbed off by the movements of the iris. Some of this material is deposited in other places in the eye including the pupillary margin, posterior cornea, and chamber angle. It also arises from the internal limiting membrane of the ciliary body and the posterior surface of the iris. Glaucoma is a direct result of this exfoliated material blocking the trabecular spaces. In the late cases where glaucoma has been present for some time, there may be a secondary deposit of material on the originally exfoliated material which piles up into the large, typical "deposits of Busacca."

The development of the secondary and tertiary zones of the frosty material has not yet been explained. I believe they are a fur-

ther degeneration of the zonular lamella. The central disc appears in photographs to be a part of the zonular lamella and to be taking part in the deterioration of this layer, in some cases by an actual peeling, in some cases merely by a change in optical density. This latter is associated with the narrow band type of exfoliation.

In treating these cases with early exfoliation, I feel at present that frequent dilatation of the pupil may be beneficial. The idea behind this is that the exfoliative material may be swept away by dilating the iris and that in doing so early in the process of the disease, the trabecular mesh may be capable of carrying it away, whereas later in the disease the already handicapped mesh may not be able to do so. In the later, well-developed cases where glaucoma is present, I feel that a filtering operation should be the procedure of choice. In cases where a definite lens opacity is present, removal of the lens should be done. The surgery in these cases does not have a particularly bad prognosis if it is done early enough.

There are still many fundamental questions to be answered, and further chemical and histochemical studies should be done. Is this a reticulin disease similar to the collagen diseases? How and why does it develop?

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ANGIOMATOSIS RETINAE, ELEVEN YEARS AFTER DIATHERMY COAGULATION*

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Presumably every ophthalmologist, neurologist, and neurologic surgeon is by now thoroughly familiar with the disease known as angiomatosis retinae (von Hippel's disease) and the commonly associated concomitant angiomas in the neurologic and occasionally visceral structures, described by Lindau (1924). The conjoint form, von Hippel-Lindau's disease, is a fascinating group of cases that are probably not nearly so rare as a survey of the literature indicates. When a clinical disease entity becomes firmly established in medicine, many cases of it are not reported in the literature unless there are unusual or atypical features.

Our ophthalmic textbooks have excellent chapters on the disease (Duke-Elder, Elwyn, Reese, Troncosco, Walsh, to name a few). Special articles are numerous (one of the best being that by Rados). It is therefore unnecessary to preface this contribution with a repetition of what is already so well known.

Although this paper is devoted primarily to a discussion of the treatment of the disease in the eye, especially by diathermy coagulation, there are however a few general items of interest that should be added. According to Duke-Elder, the first case to be reported was that of Panas and Remy (1879), followed by Fuchs (1882), Lagleyze (1884), Darier (1890), Wood (1892), Treacher Collins (1894), and von Hippel (1895, 1903), who established it as a clinical entity in 1904. To this list of pioneers in the subject should be added the name of Galezowski, whose *Atlas of Ophthalmoscopy* was published by Balliere in Paris in 1886. Prof. E. B. Streiff has recently drawn this to our attention by finding that Plate 28, Figure 1, is a classic painting of the disease. Furthermore, Galezowski's patient died of a "gliosarcomatous" tumor of the brain. This is probably the first case of von Hippel-Lindau's disease on record.

There is still some confusion in the differential diagnosis, especially in the later stages of the disease. The recognition of the retinal lesions in the early stages presents little difficulty, for the presence of a pair of enormously dilated vessels, entering or leaving a tumor that is usually located in the far periphery and that may vary in color from white or pink to red, is too striking to miss. However, multiple congenital aneurysms may cause confusion. Here both arteries and veins may be enormous in size, but there is an absence of exudation, which is part of the von Hippel entity. Later on in the course of angiomatosis, the amount of exudation, hemorrhages, and gliosis may suggest Coats's disease, or even retinoblastoma.

A. B. Reese has succeeded fairly well in clarifying the puzzle of Coats's disease for us. He shows that this is basically a more or less masked telangiectasis of the retinal vessels, with the formation of a thick homogeneous polysaccharide basement membrane under the endothelium. This often causes atresia and occlusion of the vessels, leading to formation of new vascular channels. In turn edema and hemorrhages occur in the deeper retinal layers which lead to detachment of the retina.

Recently Renard and Brégeat have described a few cases more or less resembling angiomatosis retinae. They call these "formes frustes," and they may well be variants of the condition. These included an atypical Sturge-Weber syndrome, with its

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variations, and the syndrome of Bonnet, Dechaume, and Blanc (circoid aneurysms of the retina associated with intracranial and facial circoid aneurysms), as well as a number of cases of isolated dilated and tortuous vessels, usually venous, sometimes associated with a "glial" plaque.

In the evolution of angiomatosis retinae it is convenient to separate the cases into four stages:

Stage I. Arterial and venous dilatation, followed by the formation of the angioma. May be single or multiple.

Stage II. Retinal hemorrhages and lipoid exudates producing star-shaped figures or retinitis circinata (concavity usually toward the angioma).

Stage III. Massive exudation and retinal detachment.

Stage IV. Absolute glaucoma, uveitis, and loss of the eye.

There is a variable interval between stages, and, apparently, any stage may suddenly and without much warning turn into a later one. The longest interval between stages seems to be between I and II (up to several years); the time is shorter between II and III, and shortest between III and IV.

It is interesting to note that in the cases where it is recorded, ocular tension in Stages I and II is normal, below normal in Stage III, and, of course, markedly elevated in Stage IV. The fact that the ocular tension is normal in the first two stages of the disease perhaps weighs against the vascular theory of glaucoma.

About 20 percent of the cases of angiomatosis retinae had Lindau's disease, approximately 40 percent were bilateral, and 22 percent showed a familial history including Lindau's disease (Usher). The heredity seems to be a dominant one and not sex linked. The sex incidence is about evenly divided.

The ages of the patients varied from three to 60 years, but the average age is 25. Papilledema is rare; if found, it may be intermittent and indicate some intracranial involvement. Papilledema may be found when the ocular tension is low (Stage III), and it does not necessarily indicate an elevated intracranial pressure.

Craig, et al., said "we have encountered many cases of hemangioma of the cerebellum without angiomatosis retinae." N. L. Aronson (neurosurgeon) said, "my experience and the literature show a rare association of the two lesions. Perhaps many of the reported cases were examined only by neurologists and neurosurgeons and without the use of a cycloplegic agent. This would account for missing some of the less conspicuous peripheral lesions." Then he, perhaps somewhat ruefully, admits, "I am sure that a competent ophthalmologist can see many things a neurologist might overlook."

Likewise we ophthalmologists might admit that, judging from the cases reported by ophthalmologists, relatively few have detailed neurologic findings or even a mention of the fact that the patient was examined by a neurologist or neurosurgeon. So it is a case of faulty teamwork on both sides. If this were corrected it might well turn out that the incidence of the conjoint disease is much higher than the 20 percent figure cited above.

Case report

My interest in the subject was sharply focused when on May 21, 1946, I saw a patient who had a typical angioma in the left eye. She was white, aged 40, and complained of failing vision in each eye for the last year and a half. The following notes are taken from my report of this case in 1949. Early in March, 1946, her vision in the left eye had failed perceptibly.

On January 24, 1945, her previous ophthalmologist had found pallor of the right optic disc and the corrected vision reduced to 20/100. The left optic disc was normal, but the vision was only 20/100. Field studies showed bilateral central scotoma, and a diagnosis of toxic amblyopia was made. She had been a heavy user of tobacco and alcohol, did not eat properly, and was emotionally upset over an impossible domestic situation. She discontinued the use of tobacco and alcohol, was given large doses of vitamins, especially the B complex, and seven months later her vision had improved to 20/30 in the right eye and 20/25 in the left.

On February 9, 1946, the patient complained of a shadow in the upper nasal field of vision of the left

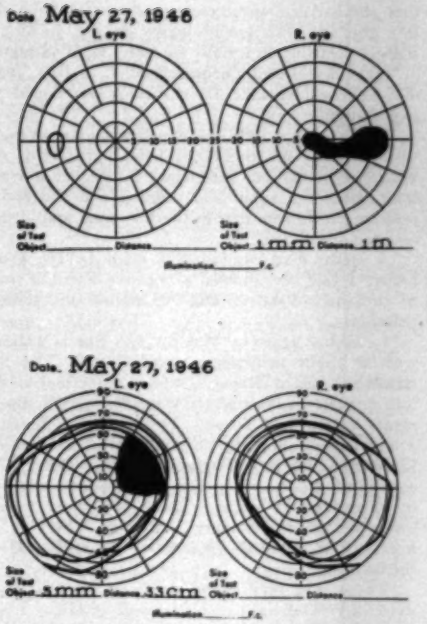

Fig. 1 (Vail). Field of vision, May, 1946.

Fig. 2 (Vail). Tumor, large vessels, and retinal lipoid changes, May, 1946.

eye. The vision was reduced to 20/70, and she said that her ophthalmologist reported a large "hole" in the retina surrounded by a lot of white spots in the lower outer quadrant of the left eye. Later she was told she had von Hippel's disease.

At the time of her first examination by me, the vision in the right eye with correction was 20/30—1, J2; in the left it was 20/70—. The right optic disc showed temporal pallor, and the central field a small cecocentral scotoma (fig. 1). The fundus in the left eye (fig. 2) showed a sharply defined, circular, cherrylike spot about one disc diameter in size, localized 18 mm. back from the limbus between the 3- and 4-o'clock positions. It was surrounded by flaky patches of exudate (lipoid). The inferior temporal vein, which was three to four times its normal size and exceedingly tortuous, ran along its usual course but abruptly took a right-angle turn to plunge into the cherrylike tumor. Branches from the superior temporal vein embraced the lesion from above. Between the lesion and the fovea was a cluster of flaky white exudate patches in all of the layers of the retina, as seen with the binocular ophthalmoscope. This cluster was arranged in a semilunar manner, the concavity toward the angioma. There were minute hemorrhages above, below, and nasally to the tumor.

On June 1, 1946, under pentothal sodium intravenous anesthesia, the sclera over the site of the lesion between the 3- and 4-o'clock positions was exposed and a single ignipuncture was made with a diathermy needle 1.5 mm. long (40 ma. for four seconds). After ophthalmoscopic verification of the accuracy of the first puncture, seven more ignipunctures were made around it. The scleral area covered was roughly three mm. in diameter. Ophthalmoscopic examination showed that the involved area was "cooked," white, and edematous, so that the outline of the "cherry" could barely be seen. There was no intraocular hemorrhage. Recovery was uneventful. The vision two months later with correction was 20/30+, J1. The site of the tumor was flat, heavily scarred, and the large blood vessel coming from below was reduced to a thin gray line. There was a slow but steady decrease in the degree of lipoid retinopathy, but it was not until two years later that all traces of the exudate had disappeared. The scar was firm, sharply defined, outlined in pigment, and there was no elevation of the retina (fig. 3). The left vision (corrected) was 20/20—.

Neurologic and psychiatric history. In April, 1947, the patient had a psychogenic crisis. She had been drinking heavily and showed some ataxia. Her physician thought she might have multiple sclerosis. An Xray of her skull at that time showed: ". . . a circular defect about one cm. in diameter located just to the right of the midline in the frontal bone. The defect communicates with the venous channel, which has no counterpart on the other side, which extends downward and slightly laterally across the frontal bone. This defect is the result of an unusually large venous channel, but it could be the result of a vascular tumor. The skull otherwise appears normal."

She was treated, however, as an alcoholic, made a splendid recovery, and all of her neurologic symptoms seem to have disappeared. There is no change

in the X-ray picture in her skull. Obviously, in view of this finding, Lindau's disease must ever be considered a possibility.

The most recent ocular examination of the patient was on April 29, 1957. The corrected vision in the right eye was 20/30, in the left 20/20—, and J1 in each eye. Ocular tension was 14.6 mm. Hg, each eye. The visual fields showed no change (fig. 4). The scar in the fundus of the left eye showed slightly more pigmentation. There was no evidence of recurrence of the original angioma or the development of new ones. The fundus of the right eye was entirely normal.

The report of the neurologic examination, May 6, 1957, by Dr. Lewis J. Pollock is as follows:

"In 1947, when I first saw the patient after you had operated on her, her complaints were a feeling of insecurity, unsteadiness in gait, and a consciousness of the left leg, and more unsteadiness in that leg. She had fallen downstairs. She also had some difficulty in starting the urinary stream. At that time, there were no objective neurologic pathologic findings.

"In 1951, although she complained of her left foot dragging, the neurologic examination was negative.

"In 1954, there was definite evidence of paresis and spasticity in the left lower extremity, and subjective sensations of tingling in the upper extremities. In November of that year there was some incoordination, paresis, and ataxia of the left lower extremity. The deep reflexes were increased, and there was a Babinski sign on the left.

"You reported a centrally placed scotoma in the right eye and asked if this might not be the result of multiple sclerosis. It was my opinion it well might be.

"In January, 1955, Dr. M. H. Wald reported that she had had three exacerbations involving the left arm and to a lesser degree the leg, in all instances clearing up usually in from 36 to 48 hours.

"Dr. Loyal Davis (neurosurgeon), in July, 1955, did not consider that the pathology warranted an exploration.

"In September, 1955, she experienced an electrical shock. When she recovered from her fright, she was able to use her left hand. I saw her a week later when she again had tingling and she had a positive Hoffmann sign in the left hand and absent abdominal reflexes.

"A spinal fluid examination, made by Dr. Wald before I saw her, showed a negative Kahn, a trace of proteins (Pandy), and 705 milligrams percent chlorides.

"I saw her again on May 6, 1957. She is walking with a slight hemiplegic, scuffing gait. The left nasolabial fold is deeper. There is more tone in the left sternocleidomastoid. Extraocular muscle movements are normal. There is no nystagmus. There is a slight rapid oscillatory nystagmus in the left eye looking to the left. There is a slight increase of associated movement in the right upper extremity on spreading the fingers. There is a slight falling away of the right upper extremity. There is no ataxia. The grasp is 80 kilos on the right; 50 on the left.

"There is a very slight ataxia in the left lower extremity. The right Achilles' jerk is brisk. There are a few clonic movements; they are more marked on the left, but the Achilles' jerk is greater on the right. The left epipatellar jerk is greater. The wrist jerks are diminished, as are the ulnars. The right biceps is greater than the left. The left triceps is absent; the right is diminished.

Fig. 3 (Vail). Lesion three months after diathermy coagulation.

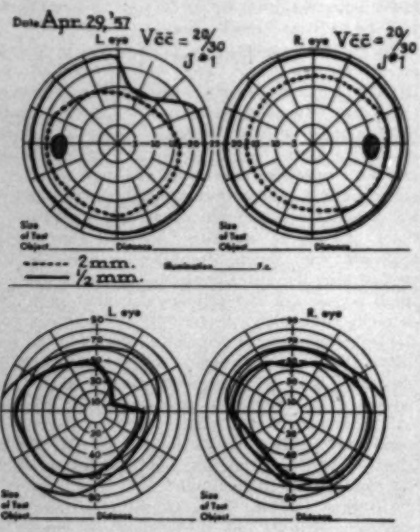

Fig. 4 (Vail). Fields of vision, April, 1957.

"There is a bilateral Babinski, right Oppenheim, right Chaddock, left Chaddock, and a left Oppenheim. The abdominals are absent. There was no loss of vibration, joint, touch, or pain sense. There was no astereognosis; no aphasia; no apraxia.

"The check reflexes are very slightly diminished.

"The bilateral signs, urinary disturbances as well as your findings are more than suggestive of multiple sclerosis."

Review of the Literature

There are five methods advocated for the treatment of angiomatosis retinae: (1) radium (Moore), (2) roentgen radiation (Cordes, et al.), (3) electrolysis (Neame), (4) diathermy (Weve), and (5) heliocautery (Meyer-Schwickerath). Of these methods, diathermy coagulation of the tumor or tumors has been the most popular, because of its many advantages. These are: ease of use; accurate, often pinpoint, destruction of the lesion; little or no damage to the unaffected parts of the eye; little delayed or remote damage to the eye; great familiarity on the part of the surgeon with instrumentation and accurate localization of the area to be treated; versatility in the use of surface coagulation as well as of penetrating ignipunctures according to indications; ophthalmoscopic observation during the procedure; no danger of producing cataract; and, as the following analysis of cases in the literature so treated shows, remarkably good and consistent results with a high percentage of perfect cures and the disappearance of exudates. The chief danger is postoperative vitreous hemorrhage.

There are cases of cures by radium (Foster Moore, et al.) and X rays (Cordes, et al.) reported in the literature. One of the most striking cures of this sort is that reported by Cordes and Schwartz before this society in 1952, when they showed a case of cure with an 11-year follow up.

On the other hand, there are cases of primary failure with radium (Handl, Neame) and with X ray (Kent, Guyton, and McGovern), where second operations with diathermy coagulation showed five successes and one failure (Guyton and McGovern).

In addition, Ballantyne reported the histologic findings in an eye that had been treated with radon seeds (4,000 r), six months later with X ray (four treatments, total 4,750 r), with vision 6/60 three months later. Two years later there was sudden loss of vision due to massive hemorrhage in the vitreous, and the development of severe acute glaucoma. The histologic studies showed more destruction (hyalin degeneration) of the normal retinal vessels than of the angioma and its feeders.

A most thorough review of the literature has disclosed reports of 47 eyes (38 patients) with angiomatosis retinae that had been treated with diathermy coagulation as the definitive or final form of treatment. The youngest patient was aged seven, the oldest 40. The average age was 25. There were 16 males and 13 females. The sex of the remaining 18 was not given.

The angiomas were monocular in nine cases, six of these involving the left eye only, and binocular in 20. The remaining 12 cases were not specified.

Thirty-nine eyes had a single angioma, five eyes showed two lesions, and three eyes showed three or more angiomas.

Most of the lesions were in the temporal periphery (14 upper temporal, 12 lower temporal). In eight eyes the tumors were in the nasal periphery, in five the lesions were directly above, and in three, directly below. Five cases were not specified.

In 10 eyes the disease was in Stage I; in 21 eyes, Stage II; in nine eyes, Stage III; although not specified in seven, it is reasonable to assume that the disease was in the first or second stage.

Ten patients (21 percent) had a family history of von Hippel or Lindau's disease or both (Saebö and Rumbauer, especially).

Nine patients had neurologic or visceral involvement, but in more than 50 percent of the cases surveyed there was no mention made of a neurologic examination.

The color of the tumors varied in description from gray white to cherry red, most of

them were noted as reddish in color. The size varied, when mentioned, from 0.5 disc diameter to 3.5 disc diameters. Most of the lesions were elevated, from 0.5 diopter to 3.0 diopters. The exudates were described as flaky or circinate but in only three cases were there star-shaped figures in the macula.

The treatment with diathermy was completely successful in 33 eyes (70 percent). Success here means total destruction of the tumor, smooth postoperative recovery, with preservation and restoration of the preoperative vision, which was very good in the majority of the cases, especially in Stages I and II of the disease. Six eyes were improved (tumor destroyed and eyeball preserved). There were eight failures, one of these (Saebö) appeared to be successful for four years, then the disease spread to other parts of the fundus, producing a detached retina and resulting in a failure. On the other hand it is probably not unusual for the postoperative reaction to persist for some time and only at the end of several weeks, or even months, to clear with restoration of useful vision (Lewis, Guyton, and McGovern).

Nine of the 38 patients had both eyes operated upon. Of these, five had a successful result in each eye and four a successful result in only one eye.

Seventeen eyes showed a postoperative hemorrhage in the vitreous (one on the eighth day, one on the 25th day); five of these were failures. Eight eyes had a temporary detachment of the retina (in four of these, the detachment was present before surgery). Five eyes had a permanent detachment of the retina (in two of these, the detachment was present before surgery). In 15 eyes the absence of a postoperative hemorrhage was definitely noted.

The period of observation of the successful cases varied from two weeks (much too short a time to be significant) to 11 years (Vail) and 12 years (Neame). The average period was less than two years.

Five eyes had multiple operations, two with success. One of the failures had a scleral resection. Three of the successful cases were treated with electrolysis followed by perforating diathermy. Most of them (33) had surface diathermy followed by penetrating diathermy, and 10 had penetrating diathermy alone (for example, Vail, Straatsma, Tsao, et al.). No cases so far as could be determined were treated by surface diathermy alone.

Most authors sought to destroy the tumor as the target of the operation. A few sought to destroy the feeders, sometimes getting into trouble. Most of them preferred to follow Weve's advice and perform a surface diathermy coagulation, immediately followed by a few penetrating points. Weve says that in multiple tumors the whole job should not be done at once; rather the necessary operations should be spread over intervals of several weeks.

In the event that the authors gave the details of their technique, which was not frequent enough, the current used in successful cases varied from 15 to 100 ma. for three to seven seconds. Obviously these figures are not of much value. It would appear however that a current of 100 ma. is unnecessarily strong and brings with it definite risks of postoperative complications. The dictum used in retinal detachment surgery, to the effect that one should use the minimum amount of current that is just enough to do the job, applies here as well.

It may be fruitful to analyze some of the failures. Rumbauer, for example, reports a case in a man aged 27 years. The right eye had been blind for a year. The left eye showed two angiomas in the temporal area. Lipoid changes were present, as well as a partial retinal detachment in the temporal periphery. Vision was 6/60. The vision on the day prior to surgery was 1/60, and the detached retina and exudate were much worse (early Stage III). Diathermy coagulation was done (50 to 60 ma., two to three sec.) into the tumors. There was blood in the vitreous, detachment persisted. Four weeks later diathermy in the area of detach-

ment was done. One and a half weeks later a third diathermy operation was done. It was followed later by scleral puncture below, which yielded dark blood. Vision was 2/60; then followed complete retinal detachment and failure.

Another example is a case of Saebö's. The left eye of a woman aged 32 had vision of 5/6. There was one angioma below. Two years later diathermy was performed, with an immediate postoperative retinal detachment and failure.

On the other hand, MacRae reported a case of two angiomas in the temporal part of the left eye of a woman, aged 27, whose right eye was totally blind. He applied catholysis (three ma. for three sec.) and surface diathermy (100 ma. for eight sec.), and short-needle perforation diathermy (40 ma. for three sec.) to the upper angioma. Immediate postoperative edema of the retina and subhyaloid hemorrhage followed. One month later a fresh vitreous hemorrhage occurred. A second operation was performed. It consisted of surface diathermy, then catholysis (three ma. for 3 sec.), followed by perforating diathermy (40 ma.); no hemorrhage occurred but much edema of the retina ensued. Two months later the lower tumor was operated upon. It was accurately localized with catholysis, followed by surface coagulation and penetrating diathermy coagulation. The final vision seven months after operation was 6/18 and "steadily improving."

An analysis of the results of surgery in the different stages of the disease shows:

Stage	Eyes	Failures	Improved
I	10	2	1
II	21	3	2
III	9	2	3
Not specified (I & II?)	7	1	

It is remarkable that four of the nine eyes that were operated upon in Stage III were successes (Weve, Tsao, Michaelson, Guillaumat). On the other hand, five failures in Stages I and II of the 31 eyes is still higher than one would like. It is possible that too much was done in these cases, that too much diathermy current was used for a particular eye, or that hitting choroidal or feeder vessels resulted in severe intravitreal hemorrhage or retinal deatchment. In six of the cases of failure, hopeless postoperative retinal detachment was responsible. There are not enough data given in the reported cases to determine with any accuracy this most important point.

There are a few additional interesting points gleaned from a study of the case reports:

1. Rumbauer includes two cases that were spontaneously healed (without surgery), thus showing that the prognosis is not invariably bad.

2. Tsao, et al., noticed that "when the eyeball is pressed with the finger the tumor becomes pale." Also, that the feeding vessels showed no branches but after operation, branches appeared. The authors believe these to be old channels reopened. Furthermore, the secondary changes (lipoid exudate, and so forth) are not entirely due to the angioma but probably result from vascular malnutrition of the retina.

3. Craig, et al., report that one of their patients had a retinal angioma that was mistaken for tuberculous focal choroiditis for some time before its proper nature was recognized.

4. Guillaumat, et al., found that the use of steroids did not help in postoperative retinal edema.

5. Straatsma found that pressing on the globe caused pulsation of the dilated vessels, but not of the tumor.

6. Guillaumat, et al., did the fluorescein test in one of their patients prior to surgery. It was normal, ruling out to some extent the possibility of an increased permeability of the capillaries in this disease.

7. Saebö remarks that "the situation is especially grave when the tumor or exudative changes take place in the central part of the fundus."

8. Möller points out that fresh angioma may develop in the retina.

9. Weve optimistically says "it appears that this disease, hitherto considered incurable, gives practically 100 percent chance of cure, provided that it is recognized in time."

10. Handl remarks that he had not seen dilated episcleral blood vessel clusters lying over the area of the angioma, either in the ciliary vascular area or in the area of the vortex veins as noted by Schreck.

11. Finally, Meyer-Schwickerath, who has devised an instrument for coagulation of the retina by light, has recently reported a case of angiomatosis retinae successfully cured by means of his instrument. His illustrations show that the tumor was totally destroyed four months after treatment. Since his method is one of coagulation, his case should be included among the successes reported above.

Summary and Conclusions

1. Angiomatosis retinae (von Hippel's disease) and its systemic counterpart (Lindau's disease) are disease entities now firmly established in medicine. They are probably more common than are supposed. Neurologists and neurosurgeons may miss the ocular lesions, ophthalmologists the systemic ones. Thus teamwork is essential.

2. Angiomatosis retinae can be divided into four stages of progression during its relentless evolution. Stage I consists of one or more dilated and tortuous veins, more or less parallel, running usually to the peripheral and pre-equatorial areas of the retina. They terminate in a circumscribed tumorous area (the angioma) which may be single or, much more rarely, multiple. Stage II consists of retinal hemorrhages, but especially of a deposit of flaky lipoid exudates scattered in the various layers of the retina. Stage III consists of massive exudation and retinal detachment, and Stage IV is terminal with uveitis, absolute glaucoma, and loss of the eye.

3. It seems to be a rare possibility that the disease may arrest itself at Stages I or II.

4. The disease is easy to recognize during Stages I and II, but Stage III may be confused with Coats's disease, advanced circoid aneurysm, multiple congenital aneurysms, or retinoblastoma. Like most familial and hereditary diseases, confusing "formes frustes" may be encountered.

5. Angiomas have been successfully treated by radium, X rays, catholysis, diathermy coagulation, and, most recently, by heliocautery.

6. This paper is primarily concerned with the treatment of this disease by electrocoagulation. Forty-six such cases (38 patients) collected from a review of the literature are analyzed. To this list is added an additional case report, 11 years after successful surgery.

7. The operation successfully cured 33 (70 percent); six were improved (eyeball saved, poor or little vision), and eight were complete failures.

8. Stages I and II are the most favorable for surgery, although it should be noted that four of the nine eyes operated on early in Stage III are considered to be successes.

9. Mild surface diathermy coagulation followed by pinpoint ignipunctures into the tumor itself seems to offer the best prospect for success. If the tumor is destroyed, the feeder vessels shrink in size and lose their tortuosity. The lipoid deposits disappear within a year thereafter. If they do not disappear, it presumably means that the tumor has not been destroyed, that others may be present, or new ones developed.

10. The greatest hazard is hemorrhage into the retina, choroid, or vitreous. For this reason diathermy should be applied with the weakest current capable of doing the job, and under frequent ophthalmoscopic control.

11. Multiple tumors are best treated separately and at intervals.

12. Sound and cogent reasons are given why direct coagulation of the tumor by diathermy or similar agents gives far better and more certain lasting results than those

reported to be obtained by X rays or radium.

13. The background statistics of this selected group of surgical cases uncannily parallel those found in the general literature of the subject.

700 North Michigan Avenue (11).

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EXPERIMENTAL IMPLANTS OF SCLERA INTO THE ANTERIOR CHAMBER*

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New York

The anterior chamber of the eye as a site for tissue implant has been extensively utilized both by ophthalmologists and cancer research workers. It is a uniquely favorable site for tissue implantation, because the implants can survive and some malignant tumor and embryonic tissue will even grow in the anterior chamber. It is also ideal for observation, because the cornea acts as a window so that the implanted tissue can be studied under magnification at will, without disturbing the implant.

Previous investigators have been concerned with changes in the epithelium, formation of epithelial cysts, the possibility of epithelization of the anterior chamber,[1-5] and the viability and growth of malignant tumor and embryonic tissue in the anterior chamber.[6-10] No one seems to have stressed degenerative changes of the connective tissue.

The purpose of this experimental study is to determine (1) the effect of aqueous on connective tissue implanted into the anterior chamber, (2) whether connective tissue implanted into the anterior chamber of the eye will eventually exhibit the same type of connective tissue degeneration as is found

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in open-angle glaucoma,[11, 12] and (3) what essential factors are needed for the development of this degenerative process.

Connective tissue from various sources, such as cartilage, cornea, and conjunctiva, was studied with these aims in mind and discarded as unsatisfactory for one reason or another. Finally connective tissue from the sclera was chosen as most suitable.

Materials and Methods

Chinchilla rabbits weighing between 1.8 and 2.3 kg. were used exclusively in these experiments. The implants could be visualized better in pigmented rabbits. Scleral implants into the anterior chamber were performed on 24 rabbits' eyes. The rabbits were anesthetized with intravenous sodium nembutal (veterinary nembutal, Abbott). A 1.5-mm. disc of sclera was removed from one eye with a trephine and immediately introduced into the anterior chamber of the opposite eye through a keratome incision near the upper limbus. Gentle stroking over the cornea with a spatula was used to move the implanted sclera into the pupillary space. The eye was atropinized in order to give the implant a large pupillary space in which to lodge.

Chemotherapy and antibiotics for the control of infection were not necessary. They should not be employed as a substitute for asepsis.

The eyes were examined with slitlamp biomicroscope, and drawings were made in selected cases. The eyes were observed at regular intervals starting with daily inspection during the first postoperative week, then every other day for two weeks, and, finally, monthly. The animals were killed at varying intervals for histologic study. The enucleated eyes were immediately fixed in 10-percent neutral formalin solution, and the anterior segments, usually exclusive of the lens, were embedded in paraffin, except for two, which were embedded in celloidin. Serial sections were stained with hematoxylin and eosin, periodic acid Schiff stain, van Gieson and Verhoeff's elastic tissue stain.

Observations and Results

A. Slitlamp biomicroscopic changes

The scleral implants were placed in the pupillary area during operation. The following day the implants were surrounded by a delicate exudate, apparently fibrin, but were still separated from the free margin of the dilated pupil in most cases. The implants showed a tendency to remain in the pupillary space until the third or fourth day after operation. When the fibrinous exudate had completely absorbed, the implant moved to the anterior surface of the iris. It was usually found in the lower nasal quadrant of the iris and appeared to be attached to its anterior surface.

On one occasion, the implant was attached to the posterior surface of the cornea. During the first few days the tissue seemed to be slightly edematous, but otherwise it appeared to be normal scleral tissue. None of the implants showed any appreciable change during the first two or three months of their presence in the anterior chamber except to become globular in shape. Of the 24 rabbits' eyes, seven of the implants gradually assumed a spongy appearance and lost their smooth surfaces (fig. 1A). This change started at the surface of the implants. There was very little shrinkage in size. The remaining 17 implants remained stationary, showing no changes in either appearance or size for the entire period of observation, the longest period being 13 months (fig. 1B).

The iris exhibited little reaction. There was some increase in pigmentation adjacent to the implant in most cases, but it was not marked. This usually occurred only after the implant had been in the anterior chamber for a few months. Occasionally the iris pigment extended to the surface of the implant (fig. 1B). No blood vessels could be seen entering the implant under slitlamp examination.

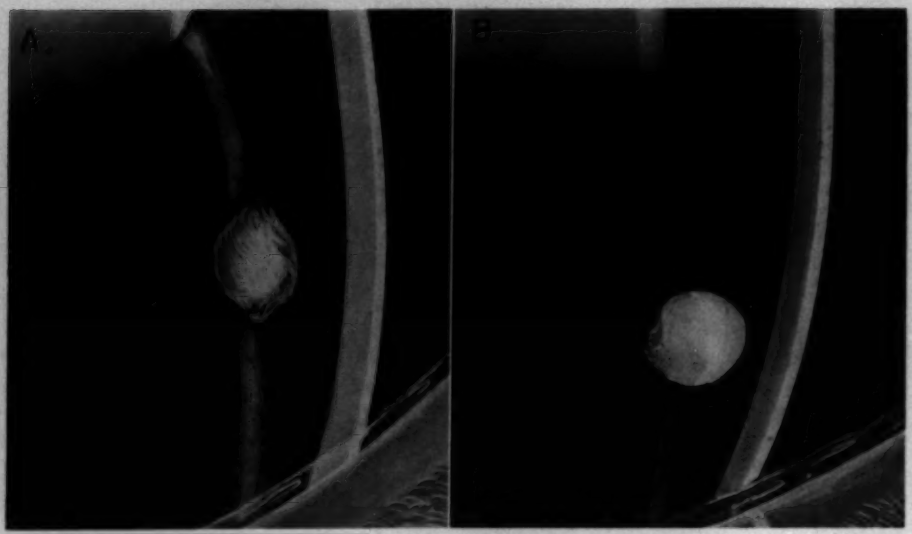


Fig. 1 (Chi, Teng, and Katzin). Drawing of slitlamp biomicroscopic picture of a scleral implant in the anterior chamber. (A) The implant, in the anterior chamber for eight months and one week, shows some sponginess, especially at the two ends (700, O.S.). (B) This implant, after 13 months in the anterior chamber, has the appearance of normal scleral tissue with a smooth surface except for some pigmentation at its base (723, O.D.).

B. Histologic changes

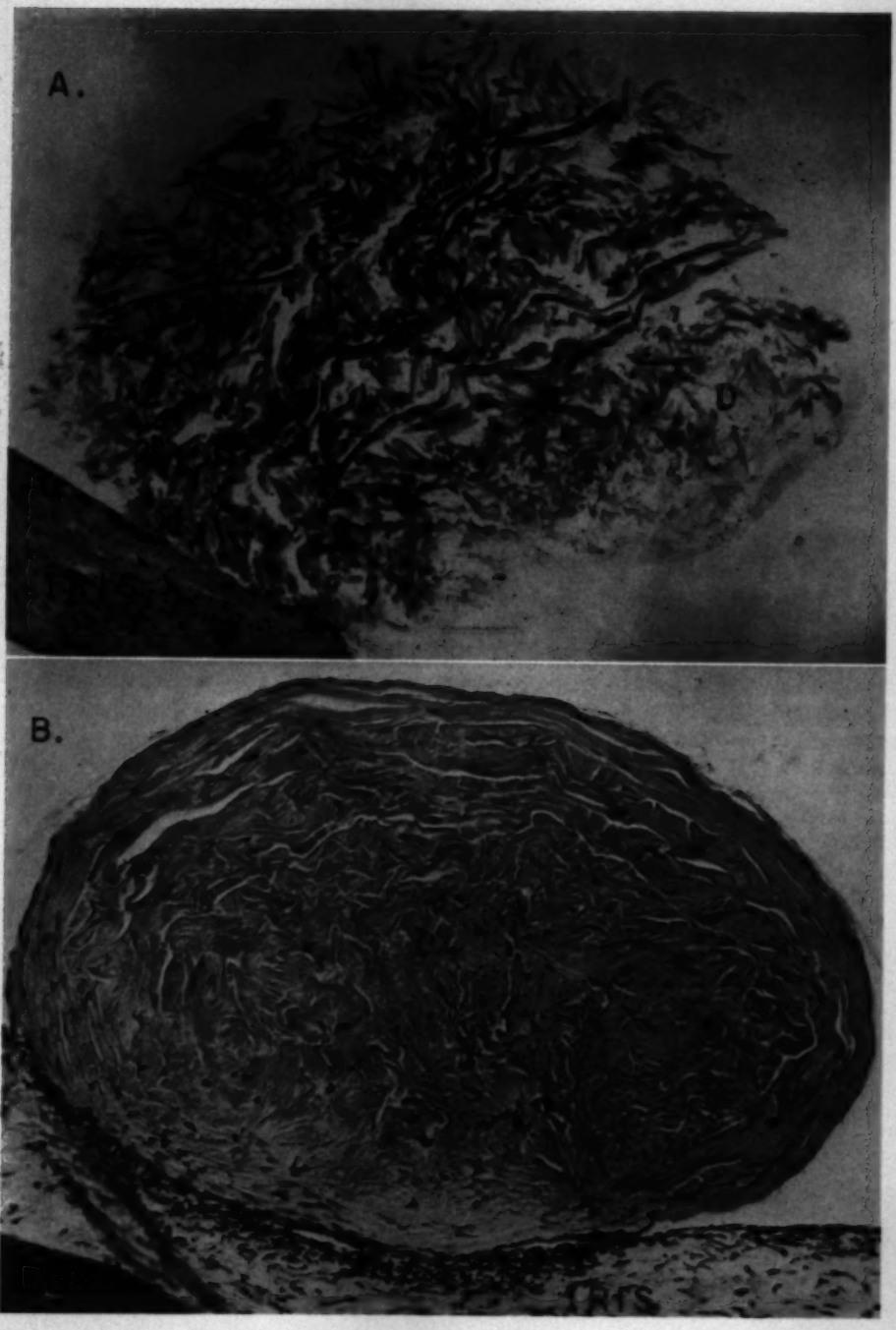
Histologically the scleral implants presented two different types of pictures: some became encapsulated in a layer of endothelial-like cells and some did not.

The seven out of 24 implanted pieces of sclera which did not become encapsulated by the cellular covering exhibited definite degenerative changes in the scleral tissue (figs. 2A and 3A). There was a decrease in cellularity with loss of ground substance and change of staining properties of the collagen fibers (figs. 2A and 3A). The collagen fibers gradually disintegrated and disappeared. The elastic fibers of the sclera were more resistant than collagen, but they also degenerated eventually. The degenerative process started from the surface of the implant and slowly extended to the center, producing the spongy appearance we had noted under slitlamp examination.

In the remaining 17 cases the implanted sclera became completely or partially encapsulated by endothelial-like cells (figs. 2B and 4). The cellular covering of the implant appeared to be a single layer in most cases, but multiple layers were occasionally seen. This cellular covering was always continuous with the surface of the iris. In one specimen there was a thin, homogeneous membrane beneath the cellular covering which was periodic acid-Schiff positive (fig.

→

Fig. 2 (Chi, Teng, and Katzin). Two different types of histologic changes occurred in sclera implanted into the anterior chamber. (A) This sclera (I), in the anterior chamber for eight months and one week, is not encapsulated by cells and shows degenerative changes with decrease in cellularity, loss of ground substance, and disintegration and disappearance of collagen fibers, especially in area D (×85, 700-7, O.S., hematoxylin-eosin). (B) This sclera (I), in the anterior chamber for 13 months, is covered by a single layer of endothelial-like cells and exhibits no degeneration of the scleral tissue (×98, 723-37, O.D., hematoxylin-eosin).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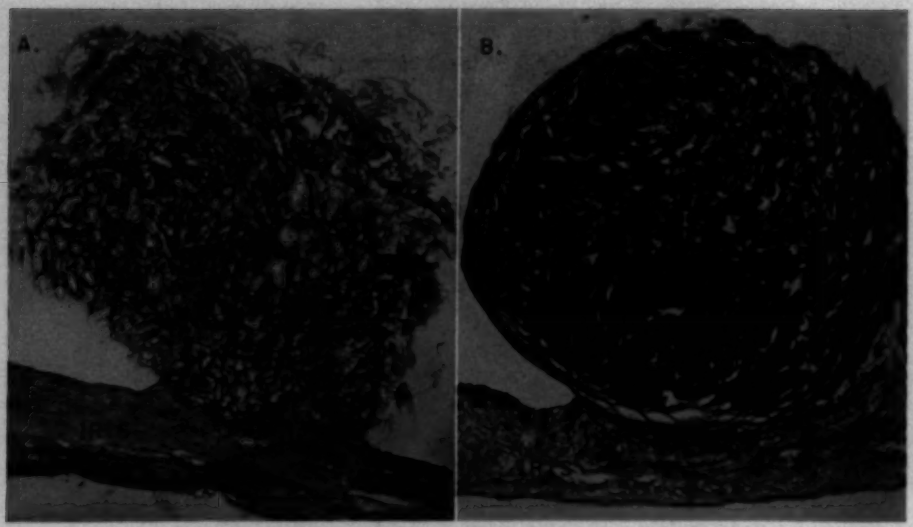

Fig. 3 (Chi, Teng, and Katzin). (A) This implant, after three months and one week, shows degenerative changes. It is not covered by endothelial-like cells and takes connective tissue stain very poorly as compared with B (×90, 693-37, O.S., van Gieson). (B) This implant (I) is encapsulated by cells after three months in the anterior chamber. There are no degenerative changes (×90, 694-27, O.S., van Gieson).

4). The encapsulated implant lived almost unaltered for the duration of the experiment (13 months). Clinically these implants appeared as normal scleral tissue with a smooth surface (fig. 1B). The time necessary for complete encapsulation of the implant varied. It was impossible to determine clinically, but histologic examination of one eye removed six days after the operation showed that the implant was already completely covered by endothelial-like cells.

All the implants, both encapsulated and nonencapsulated, were attached to the anterior surface of the iris, except for one

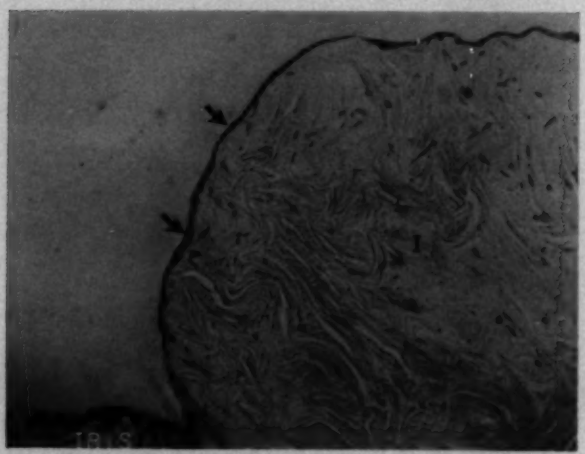

Fig. 4 (Chi, Teng and Katzin). In this specimen the sclera (I) was in the anterior chamber for nine months. It is covered by a single layer of cells and a thin, homogeneous membrane which is positive to periodic acid-Schiff stain (arrow). It shows no degeneration of scleral tissue (×112, 721-48, O.S., periodic acid-Schiff).

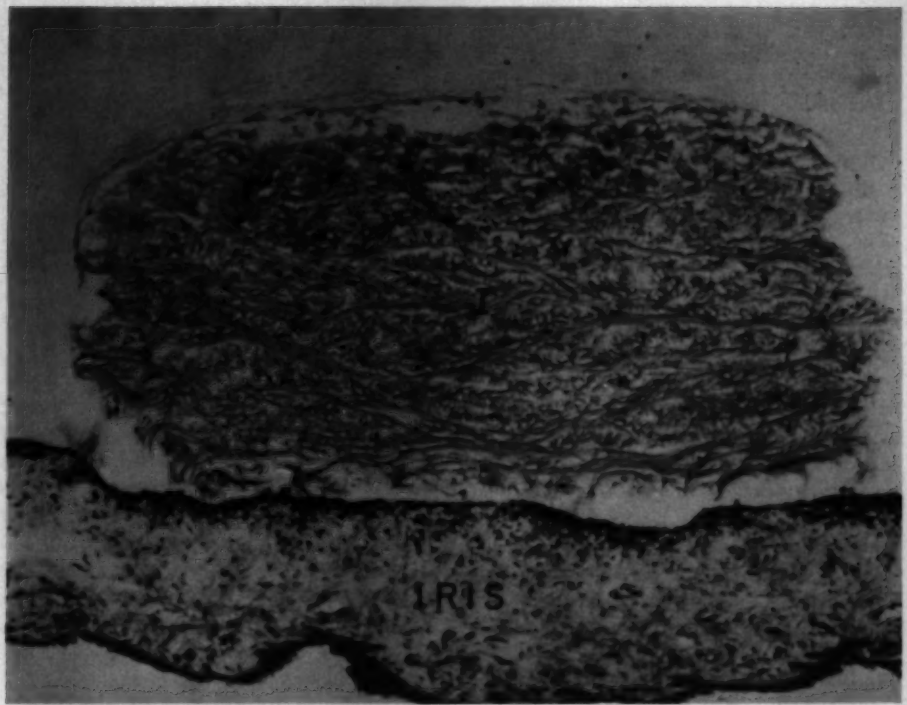

Fig. 5 (Chi, Teng and Katzin). This implanted sclera (I), in the anterior chamber for two days, appears slightly edematous and its anterior surface is covered with a delicate fibrinous exudate containing macrophages (×85, 830-25, O.D., hematoxylin-eosin).

specimen in which the implant had accidentally adhered to the posterior surface of the cornea. There was slight, but consistent increase in pigmentation of the iris underlying and adjacent to the implant after the implant had been in the anterior chamber for a few months (figs. 2B and 3B). There was no infiltration of inflammatory cells or invasion of blood vessels, either in the encapsulated or the nonencapsulated implants.

Within the first few days the implants were surrounded by delicate fibrinous exudate containing some macrophages and some stellate cells (fig. 5). The latter were probably fibroblasts transformed from the macrophages. The implants became slightly edematous, but did not otherwise look appreciably different from normal sclera.

Comment

Comparison of the slitlamp biomicroscopic and histologic appearances of these specimens showed that the implants with smooth surfaces were those that had become encapsulated by endothelial-like cells, while the spongy look of the nonencapsulated scleral implants was due to degenerative changes. This experimental work strongly suggests that cellular covering of the implant plays an important protective role in preventing the degeneration of the connective tissue implanted into the anterior chamber. Gundersen[2] reported that one of his corneal implants was covered by proliferated corneal endothelium and the corneal stroma lived almost unaltered in the anterior chamber for 20 months.

The cellular covering of the implanted sclera is so delicate that it cannot be detected in the living eye with the slitlamp. There was nothing in the technical procedure in the cases that developed encapsulation which differed from that in which the implants did not become encapsulated. We have no satisfactory explanation for the encapsulation in some cases and the nonencapsulation in others.

In this investigation the cellular covering of the implant most likely originated from the endothelium of the iris. In most instances the encapsulated implants were covered by a very delicate unicellular layer which appeared to extend from the iris surface, made up of cells continuous with and not distinguishable from the iris surface endothelium. Sometimes it is associated with pigment extending from the iris surface. As Snell[13] pointed out, the endothelium of the iris surface shows some capacity to proliferate. Another possibility to be considered is that these cells originate from macrophages which are present in the fibrinous exudate in small numbers during the first few days. Later these macrophages are transformed into fibroblasts, but show no tendency to lay down collagen. On the other hand, in one specimen, there is a thin, homogeneous membrane under the cellular covering which takes positive periodic acid Schiff stain. It seems that this is a basement membrane formed by the endothelial-like cells. Based on morphology alone, it is difficult or impossible to distinguish endothelial cells from fibroblasts.

It is interesting to note that vascularization does not occur in scleral implants, although other tissue implants (cornea,[2] conjunctiva,[5] cancer,[6-9] and embryonic tissue[10]) were always invaded by blood vessels from the iris.

The degenerative changes in the nonencapsulated scleral implants may be due to the presence of certain substances in the aqueous, affecting the implant directly. It is also possible that the degeneration is due to the continuous leaching-out of the ground substance of the implant by the aqueous. The change in the ground substance may create an unfavorable environment for the implanted sclera to live normally. In either case, our work shows that the cellular covering has a very important protective function toward the implanted sclera. This study lends a great deal of support to our previous observation of primary degeneration in the vicinity of the chamber angle in open-angle glaucoma.[11, 12] We pointed out that the degeneration probably started with the endothelial lining of the trabecula around Schlemm's canal. The degenerative change in the endothelial cells caused greater exposure of the other elements of the trabecula to the aqueous, leading to degenerative changes in those elements. The healing or reactive phase of the degeneration was marked by proliferation of the endothelium from the remaining normal cells. Both the degenerative and the proliferative processes contribute to the decreased facility of aqueous outflow.

Summary and Conclusion

Autologous scleral implants in the anterior chamber of rabbits' eyes can survive without change for periods up to the duration of this experiment (13 months) if encapsulated by endothelial-like cells. The nonencapsulated implants reveal degenerative changes which are strikingly like those found in open-angle glaucoma. This suggests that cellular covering of the implant plays an important protective role in preventing degeneration of the connective tissue implanted into the anterior chamber. This experimental work strengthens our theory that in cases of open-angle glaucoma, changes in the endothelial cells of the trabecular meshwork may result in a greater exposure of the other elements of the trabecula to the aqueous, and this, in turn, causes the degeneration of these elements.

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PENETRATING KERATOPLASTY*

Observations based on a series of 148 cases with special emphasis on techniques of graft fixation

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Introduction

Transplantation of the cornea is undoubtedly one of the most fascinating subjects in modern ophthalmology. During the past 19 years, I have had the opportunity of doing 148 of these grafts, principally at the Massachusetts Eye and Ear Infirmary and St. John's Hospital, Lowell. The statistical results of cases from the ward service of the Massachusetts Eye and Ear Infirmary before 1947 were included in the report on corneal transplantation sponsored that year by the American Academy of Ophthalmology and Otolaryngology. The Lowell cases, however, which include those from active ward services and all my private cases, have not been reported previously. Using this series with its extremely diverse results as a background, I would like to emphasize a few points on transplantation which experience indicates to be of more than ordinary interest or importance. A statistical analysis will also be included of 100 consecutive transplants done during the years 1944 to 1954.

Classification of transplants

Transplants are classified in two ways, by surface area and by depth (fig. 1). According to area, they are total if the entire width of the cornea is used, and circumscribed, or partial, if only a window is taken from the cornea. According to depth,

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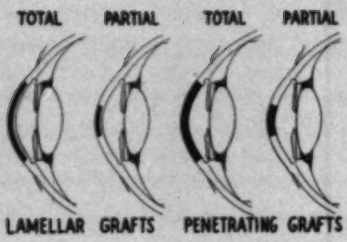


Fig. 1 (Leahey). Classification of grafts.

they are lamellar when only the top layers or lamellas are replaced, and penetrating when the full thickness of the cornea is transplanted. Thus one recognizes four types: total and partial lamellar, and total and partial penetrating keratoplasty. Until a few years ago only the partial penetrating was considered of value; but lamellar grafts are now widely used also.

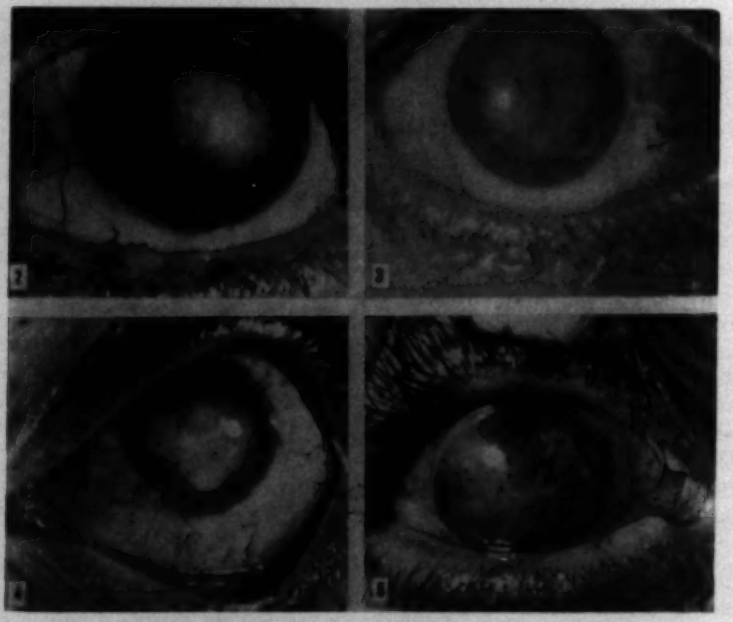
Selection of cases

The first key to success is the proper selection of cases. Favorable cases are those in which the eye is normal except for the cornea; the leucoma, or scar, is not dense or vascular; and there are areas of clear or slightly scarred cornea surrounding the graft to furnish it nutrition (figs. 2 and 3). Especially unfavorable cases are those with dense scarring of the entire cornea, vascularized pannus from old trachoma or severe chemical burns (fig. 4), and edema of the cornea as in Fuchs's dystrophy (fig. 5). In my experience the "most favorable cases" have been the following groups in the order listed: (1) small central scars from any cause, (2) keratoconus, (3) Groenouw's familial dystrophy and lattice keratitis, (4) diffuse thin scarring as from old phlyctenular keratitis, and (5) old interstitial keratitis with irregular moderate scarring.

Preparatory treatment and considerations

Corneal blood vessels

Many eyes that are otherwise hopeless can be made suitable for grafting by pre-



Figs. 2 to 5 (Leahey). Scar types. (2) Central, very favorable. (3) Old disciform, favorable. (4) Vascularized lime burn, unfavorable. (5) Fuchs's dystrophy, very unfavorable.

liminary surgery. One of the worst problems is getting rid of the blood vessels. Some of these vessels can be closed by means of cautery or diathermy applied to the vessels at the limbus for two mm. I have done a very large number of these, and, in general, my results are unsatisfactory. Nine out of 10 of the vessels soon reopen. Corneal stripping (superficial keratectomy) is helpful when the vessels are large and superficial; but, again, the results of stripping are disappointing. Radiation is the most effective method.

Since radiation works well only on small vessels and new capillaries, the larger trunks should still be treated by stripping or diathermy peritomy. Radiation may be given in many ways. Since 1948, I have been using a 23 mc. radium D applicator and consider this the most satisfactory method to date. These applicators are much more expensive than the other available beta ray applicators, costing several times as much as strontium 90. The radium D beta rays have less penetrating power than those of strontium 90, radium, and radon, and the rays are almost completely absorbed in the corneal tissue. Since less than a fourth as much radiation from radium D reaches the lens surface as from the other applicators, it is particularly safe and suitable for corneal treatment, and is unquestionably the method of choice for superficial corneal vessels.

Some ophthalmologists[1,2] have reported radium D ineffective in treating corneal vascularization. My applicator has been used for a total of about 2,000 treatments on approximately 300 people for corneal vascularization of many types including a great many cases of rosacea keratitis, recurrent pterygium, and chemical burns. In practically all of these cases the radium D proved extremely effective even when there was deep vascularization. About one third of the cases with deep vascularization had some temporary irritation of the eye during the treatment, but ill effects were rare. Approximately two percent of the radiated corneas showed delayed superficial ulceration of the cornea lasting several months. The few eyes so afflicted originally had full thickness dense leucomas with extremely extensive deep vascularization, and each also had a preliminary superficial keratectomy followed by more than the customary dose of beta. Thus far no cataract which can be attributed to radium D has been observed. Other authors, however, have recently reported numerous radiation cataracts following use of strontium 90, radium, and radon applicators.[3-6]

No one applicator can be best for all situations, and in the light of present knowledge the ideal therapy would be to use radium D on eyes with vascularization primarily in the anterior two thirds of the cornea. The more dangerous applicators with deeper penetration (strontium 90, radon, or radium) could be substituted for radium D in the relatively small group of cases with vessels abundant in the posterior cornea.

Immediately after the first beta treatment, a diathermy peritomy is done on any large vessels running across the limbus into the treated area. When doing the peritomy it is desirable to wear a magnifying loupe, and to regulate the current so that the vessel is coagulated without causing any measurable burn to the surrounding tissues. For peritomies done in the office a Britcher Hyfrecator is very satisfactory. The needle should be in contact with the cornea before turning on the current to avoid making a spark gap and causing superficial burn outside the vessel area.

Since with a 23-mc. radium D applicator each five-mm. area of vascularization requires about five six-minute treatments, mechanical holders are desirable. The Stevenson holder, which attaches to the speculum, is rather difficult to adjust; and with it, slight motion of the speculum is enough to allow the applicator to rub on the cornea. A few years ago, I designed one consisting of a malleable wire which slides into holes in an eye glass frame or headband (fig. 6).

Fig. 6 (Leahey). Holder for beta-ray applicator.

The wire is set in place over the desired area of the cornea and the fine adjustment is made on an easily turning screw at the radium end of the wire.

Under the slitlamp, the radiated corneal vessels appear to undergo an obliterative endarteritis. They get smaller in caliber, darker in color, and frequently show little hemorrhages along their course. Later, short sections of the vessels disappear completely. The effect is usually not complete until three months after the last treatment.

Complete corneal pannus

When there is extensive thick pannus of the cornea a superficial keratectomy is done, and the conjunctiva and scar tissue are resected for four mm. back of the limbus (figs. 7A, B, and C). The sclera is scraped bare and free of vessels in much the same manner as when transplanting a pterygium. It was formerly thought that complete recession of the conjunctiva all around the limbus, leaving the sclera bare, would cause interference with corneal nutrition and possible serious corneal damage. In 1947, however, Lombardo[7] showed that this method was often helpful in removal of extensive pannus in trachoma and caused no damage to the cornea. I tried his method in a few cases, but did not find it effective until it was combined with radiation.

The cut edges of the conjunctiva are held in position by four silk sutures passed through episcleral tissue. Three days after, beta radiation is started before the vessels have time to grow in again. Incidentally, it is very difficult to do an extensive corneal

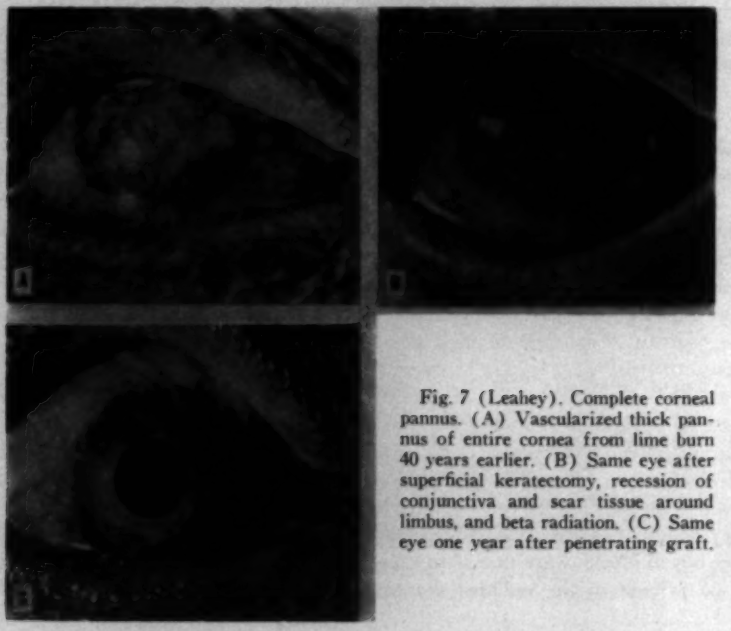


Fig. 7 (Leahey). Complete corneal pannus. (A) Vascularized thick pannus of entire cornea from lime burn 40 years earlier. (B) Same eye after superficial keratectomy, recession of conjunctiva and scar tissue around limbus, and beta radiation. (C) Same eye one year after penetrating graft.

stripping with a cataract knife or an ordinary surgical knife such as the Bard Parker No. 15. The process is greatly simplified by using the gently rounded blade of a sharp Demarres corneal splitter similar to that frequently used in lamellar keratoplasty. Where this is not available the round tipped Beaver No. 44 blade is moderately satisfactory.

Extreme keratoconus

In some severe keratoconus cases there is rupture of Descemet's membrane and acute ectasia of the cornea. In two cases in this series this was extreme. The entire cornea in one case was edematous and white, and vision was reduced to light projection only. In both cases, elastic pressure bandages worn constantly for several weeks reduced the ectasia, and the edema gradually cleared completely. In the worse case there was no keratoconus three months later, but the entire cornea was semi-opaque and a number of small vessels had grown in due to the keratitis. Following beta radiation both of these eyes were suitable for grafting.

Some surgeons advocate reducing the marked keratoconus by cautery at the apex before grafting. This flattens the cone, but unfortunately it often causes marked vascularization of the cornea. In general, this therapy is not to be recommended.

Synechia

Anterior and posterior synechias should be released when possible and the pupil made dilatable, as otherwise anterior synechias may form at the edges of the new graft. A preliminary iridectomy may be needed in some cases.

Location of graft

The location for the new graft should be picked carefully. It should be in an area that leaves as much clear cornea for its border as possible. This is of great benefit to the nutrition of the graft; and, in fact, the amount of healthy corneal tissue at the graft margin is probably the most important single factor in determining the ultimate success of the graft.

The graft should also be located so that it will lie within the pupillary area or the opening formed by the pupil plus the preliminary iridectomy in order to lessen the chance of anterior synechias.

In keratoconus cases it is desirable that the entire thin part of the cone should be removed so that the edge of the graft will be in contact with host cornea of at least 60 percent normal thickness. This generally calls for a graft at least six mm. in diameter with the center often slightly down and to the nasal side.

Size of graft

The size of graft preferred in ordinary cases varies with the surgeon and with the size and shape of the corneal scar, but most of mine have been from 4.5 to six mm., with the great majority being five mm. in width. The five-mm. graft is also most widely used by other surgeons. The smaller the grafts, the less the chance of dislocation and anterior synechias, so before the advent of direct sutures a 4.5-mm. graft was desirable for patients whose postoperative behavior we distrusted, or for eyes in which the pupils could not be dilated.

There are two main disadvantages to small grafts. If additional direct sutures are desired, inserting these sutures in the graft is much more difficult than in a large graft, and the suture track also encroaches on a larger percentage of new cornea. In addition, when there is proliferation of tissue on the back of the graft, or edema of one edge due to slightly defective union, the pathologic process has a shorter distance to go to affect the center of the graft and visual acuity. Judging from my cases, another disadvantage, much less important, is that the average residual astigmatic error is greater in smaller grafts than in large ones, presumably because any irregularity becomes greater in relation to a smaller diameter and thus causes a greater change in curvature.

The disadvantages of the larger grafts are the need of direct sutures, increasing tendency for anterior synechias and their attendant complications, increasing tendency for poor coaptation in one area or for bulging of the entire graft, and, in very large grafts, increasing tendency for vascularization due to proximity of the graft margin to the limbus.

Miscellaneous factors

If a cataract is present, the graft should be done first and the cataract removed about four months later, as the chance of a successful graft in aphakic cases is very slight. Following the transplant a cataract extraction is no more difficult than on a normal patient. Former glaucoma cases must be under complete control without miotics. Nystagmus is not necessarily a contraindication.

The donor

Condition of the donor

It is generally agreed that cadavers provide as satisfactory material as living subjects. Blood grouping and systemic diseases appear to make no difference. In the light of recent work on possible tissue sensitivity, it is probable that some incompatibilities will eventually be found. Randolph (1949) in experiments on rabbits decided that it is practically impossible to transmit syphilis in the graft.[8] Despite this work, however, in the United States corneas are usually not accepted for transplantation unless the donor has had a negative blood test. The eyes are also considered unsuitable when death is from an acute infection or from blood dyscrasias such as leukemia.

The eye, of course, should be free from inflammatory changes and from any suggestion of corneal dystrophy. In earlier years I used several eyes enucleated for painful glaucoma. These corneas are apparently satisfactory if the edema has been of short duration and it is still possible to clear the cornea with glycerin or hypertonic saline. Arruga,[9] Filatov,[10] Wright,[11] and Paton[12] also consider these glaucoma eyes satisfactory. Since the corneal nutrition is abnormal following several days of edema, however, and since corneal material is now more plentiful, I have used no glaucomatous eyes during the past 10 years.

A similar situation exists in regard to malignant tumors in the posterior segment of the eye. I formerly used eyes with malignant melanoma of the choroid provided there were no aqueous or corneal changes by slitlamp. Many surgeons[12] consider this safe; and as yet there has been no case in the literature of a melanoma recurring in a recipient eye. Since a single cell on the back of the cornea might spread the malignancy, however, I feel it is unwise to use these eyes, and this opinion is shared by many other surgeons. Retinoblastomas are more malignant and spread more quickly, and since Hata[13] reported a case in which a retinoblastoma again occurred after keratoplasty, most surgeons reject all such eyes.

Recently, I successfully utilized the cornea of an electrocuted convict, an experience which has also been reported by other surgeons.[14] These corneas appear satisfactory, provided there is no visible corneal opacity.

In general, autoplasty (from same individual) has no advantage over homoplasty (from same species). Blumenthal[15] reported a successful graft from a Negro to a white person. Because of the possibility that delayed edema of the graft may be due to tissue sensitivity, it is reasonable to expect, however, that autogenous grafts will ultimately be proven more successful. Heteroplasty (from one species to another as from cat to man), despite some temporary success, has never given a satisfactory result in animal or man.

Age of the donor

Many years ago when beveled grafts were more widely used, the eyes of newborn

babies were frequently utilized. I consider these very unsatisfactory for our present method with nonbeveled implants, and this opinion is shared by most surgeons.[12, 15, 16, 17] Babies' corneas are thinner than those of adults. Because of their limpness, there is far more danger of poor union or postoperative bulging. Because of their short radius of curvature, they also tend to cause high myopia. Vannas[18] claims that a contact lens is often necessary to correct this resultant myopia.

The eyes of young children are satisfactory, but possess to a lesser degree the disadvantages of infants' corneas. From adolescence to the age of about 70 corneas appear to me to be especially suitable. In general, the cornea tends to be stiffer in the older person and therefore is easier to manipulate when a large size graft is used; it also is more apt to stay exactly in place. Elschnig,[19] Thomas,[20] Lohlein,[21] and McLean[22] consider the age of the donor of little significance. Barraquer,[23] Franceschetti and Bischler,[24] Filatov,[10] and Paton,[12] however, believe corneas from old people are superior.

There is no evidence available as to the relative value of corneas from extremely old people. Since very elderly corneas transmit less light than those of younger people, and since senile corneal tissue in life is more prone to a number of degenerations, extremely old corneas should be considered less desirable until proven otherwise.

Methods of preservation

The usual method of preservation in the United States is to refrigerate the eye at ordinary ice-box temperature (4°C.). It may be kept in normal saline if it is to be used within six to 10 hours. If it is to be kept for a longer period, it should be in a sealed moist chamber with gauze and saline in the bottom. The cornea is upright and is not covered by the fluid.

In Europe, refrigeration in liquid paraffin is preferred by many surgeons.[25–30] Success has also been reported in preservation by partial dehydration[31] of the cornea and reconstitution with saline shortly before grafting, and by freezing.[32]

Most surgeons, and probably all in the United States, preserve the entire eye. Vannas,[18] Amsler,[33] and a few others, however, take only the cornea. This considerably simplifies the procedure in acquiring donor grafts, as no enucleation is required when the cornea is taken from a cadaver.

Length of preservation

Most surgeons[34–36] believe that for penetrating keratoplasty the graft should be utilized as soon as possible, and the earlier after death the eye is used the better. Fialho[37] found that, in eyes preserved in liquid paraffin, opacification started on the posterior surface after 24 hours and was complete by the seventh or eighth day, but the process was more delayed the sooner after death the eyes were removed. Petrossian[38] reports that eyes preserved in saline and studied under a microscope show a similar course. They begin to degenerate very soon, but are transparent despite irregular epithelial lesions up to the eighth or 10th day. On the 15th, they are semitransparent and on the 20th completely opaque.

In my own experience, the eyes tended to get soft in 12 to 18 hours, and when examined with an ophthalmoscope and corneal microscope they showed progressive wrinkling of Descemet's membrane and irregular epithelial deterioration. When the intraocular pressure was increased by squeezing, most of the folds in Descemet's membrane disappeared. In some eyes the corneas remained semitransparent as long as 25 days.

In all the early cases of this series (those preceding the 100 cases tabulated), eyes enucleated from living people were employed and the transplants were done within one to three hours. When the Eye-Bank was first started, I used corneas up to 24 hours old. After using one cornea with markedly wrin-

kled Descemet's membrane, however, similar folds remained permanently in the otherwise transparent graft; since then I have tried to use material less than 20 hours old. Most surgeons, however, use tissue up to 24 hours, and many up to 48 hours, after death. There are no satisfactory statistics to prove definitely the relationship of this time interval to graft success, but it is my impression that my results have been better when this period has been very short.

Filatov[39] in Russia takes a diametrically opposite viewpoint. He thinks aging of the graft in refrigeration for four days causes changes in the tissue which improve the biologic qualities of the transplant and make it less able to react unfavorably to so-called "tissue sensitivity," thus resulting in fewer cases of delayed edema of graft. Some French surgeons, including Paufique and Sourdille,[40] have followed his teaching in this matter but are not definitely convinced. They do, however, agree that preservation for several days appears definitely beneficial in the case of lamellar grafts.

Technique

Preliminary considerations

I have tried many different techniques, but from 1937 to 1944, 90 percent of my cases were done with beveled edges by the square method of Castroviejo. About that time, along with other American surgeons, I realized that the use of nonbeveled grafts, as long advocated by Filatov, actually was a sound and practical surgical method. A switch to round grafts followed, and with these the operations have been in general much easier and more satisfactory. The advantages of a round graft are many:

1. When stained with fluorescein, the outline of the circle is always much more visible than the square marked by the knife. This is a great help when inserting sutures or finishing the cutting of the graft.

2. After the sutures are inserted, the trephine can be reapplied with much less danger of a false incision than with the double knife. A double knife, incidentally, often spreads slightly during the incision, so the cuts are not strictly parallel.

3. With the round graft, no keratome incision is necessary. In cases with dense leucoma this keratome incision is a delicate procedure, as too shallow an incision will split the corneal lamellas, and too deep a one may injure the lens.

4. After the anterior chamber is opened, excision of the remainder of the graft by scissors is much easier with the round graft, as a trephine cut can be safely made much deeper than a knife cut.

5. Elimination of the corners of the graft reduces the danger of anterior synechias.

There are occasional cases, however, in which, due to the configuration of the scar, a square graft may provide more clear cornea at the graft margin, and in these the square method may still be desirable.

Preliminary medication. An enema is routinely ordered. For sedation Sodium Amytal 100 mg. is given one and a half hours prior to surgery and Demerol 50 mg. one half hour before operation. The pupil is widely dilated with instillations of one-percent atropine one and a half hours and one hour before operation, and two drops of 10 percent Neosynephrine 15 minutes before operation.

With grafts over six mm. in diameter, it is difficult to keep the pupils dilated enough to prevent formation of anterior synechias. In these cases, instead of mydriasis, preliminary miosis is obtained with pilocarpine or eserine. Since the margin of the pupil adheres to the graft edges more readily than do other areas of the iris, it is safer to keep the pupil inside the graft area for the first 24 hours rather than near its border.

Anesthesia. Three drops of one-percent Pontocaine and three of four-percent cocaine are instilled at one-minute intervals just before the operation. A Van Lint-type injection of two-percent Novocain with adrenalin is given in the orbicularis fibers of the lid and under the skin for three cm.

external to the outer canthus. If the patient has a small palpebral aperture or is nervous, the tissue of the outer canthus is crushed in the tip of a hemostat for about five mm. and a bloodless canthotomy is then done with Stevens tenotomy scissors. A small amount of Novocain-adrenalin solution is injected subconjunctivally over the insertions of the four rectus muscles. No hyaluronidase is used and no retrobulbar injection is given, as the soft eye so desirable for some other surgical procedures is a complication in keratoplasty until after trephining is completed.

In aphakic cases, however, retrobulbar injections and pressure on the eye for several minutes are advantageous. With the lens already out there is no danger of hurting it with a trephine, and with a soft eye there is less tendency for vitreous prolapse to occur. In nonaphakic patients, also, if the eye is moving too much, a retrobulbar injection may be given after penetration of the chamber by the trephine before excision of the disc is completed.

Speculum. In earlier years I used a Guist speculum, but later I found the Arruga type much more satisfactory. Like the Guist model, this also has little foot plates which hold the lids off the eyeball, but the Arruga type allows more working room between the eyelids. I have modified the Arruga speculum with a third "foot plate," adjustable on the lower cheek, which can be slipped on for rare cases where the lower lid still shows undue pressure on the eyeball. Lid sutures or lid clamps are also satisfactory.

Choice of trephine. Automatic trephines, which I have used in a number of cases, usually take the button out without need of scissors. There are certain disadvantages to these, however, and I continue to favor the more deliberate hand trephine. My two automatic trephines have blades fashioned by renowned instrument makers. Despite this, the majority of the blades when tested lightly against epithelium show a slight "shimmy," indicating a microscopic defect in the axis of rotation. In some cases this leaves a rather wide line of epithelial abrasion instead of the fine cut expected.

With the hand trephine, minute defects in the angling or centering of the trephine handle are immaterial. The trephine is being rotated back and forth in a groove instead of being spun around, and it remains in its own original track. Most surgeons prefer the hand trephine, but there are some dissenters, including Arato,[41] whose instrument works in a guide supported from the limbus, Vannas,[18] Boase,[42] and Lohlein.[21] The latter reports a considerably higher proportion of clear grafts from a mechanical than from a hand-driven trephine.

I prefer the old-style Castroviejo trephine with open sides and no central plunger. This allows full visibility of the corneal button, and, when working on a recipient eye, a central control suture from the corneal button can be pulled up and out through the window of the trephine.

All regular trephine handles have certain disadvantages, chief of which are lack of flexibility and slowness in rotation. For years I have put a one-inch piece of No. 10 rubber catheter on the top of the trephine shaft, and I find this makes a perfect handle. It is satisfactorily flexible, and due to its very small diameter more rotation is obtained with less finger motion.

Methods of graft fixation and postoperative care

Of the numerous changes being continually made in techniques, by far the most important recent advances have been in the field of fixation of the new graft.

In general, presently advocated fixation methods may be divided into four types: (1) overlying bridge sutures, (2) overlying splints, (3) direct sutures, and (4) fibrin fixation.

Before considering actual methods, it should be emphasized that perfect fitting of the graft is one of the most important factors in obtaining good fixation. The success

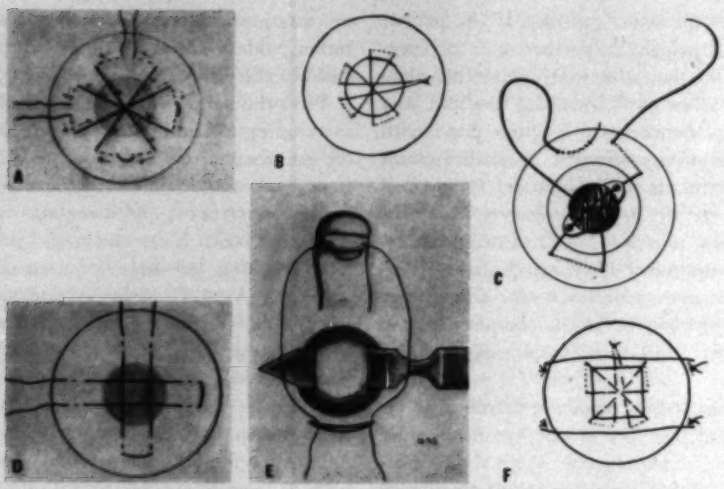


Fig. 8 (Leahey). Suture methods. (A) Thomas. (B) Castroviejo. (C) Paton. (D) Bietti. (E) Filatov. (F) Sutures plus conjunctival flap (1937).

of any given suture method, therefore, varies widely with the accuracy of the cutting technique. It is generally recognized that the round graft is a more accurate fit than the square one, and it is technically easier to do; most routines at present call for a round nonbeveled transplant.

If the graft is a good fit, the edges should be air tight immediately following operation. In these cases new endothelium and epithelium grow across the edges in 24 hours. If there is slightly defective apposition only in some areas, serum and fibrin usually fill the gaps and fibroblasts soon grow in leaving a broader scar than do perfectly apposed edges.

The margins are not united firmly for a month,[34] but in the absence of unusual trauma or pressure, the graft should hold without further use of sutures after six days. Since the first few days are crucial, the essential point in fixation is to provide steady apposition of the margins for at least that period.

Overlying sutures. Until recent years, all really successful techniques employed some variation of overlying sutures, and these bridge sutures are still widely favored for small grafts.

The original von Hippel technique of 1887[43] was a partial lamellar keratoplasty done with a mechanical trephine. No sutures were used, and the graft was kept in position by pressure of the eyelids only. In 1905 Zirm[44] did a full-thickness graft by von Hippel technique, but the graft was held in position by two cross sutures inserted in the conjunctiva above and below. Since that time the trend has been toward an increasing number of sutures, and the sutures now are firmly anchored in the cornea about one mm. from the graft margin and are carried across the graft to hold it in place.

Thomas, in England, originally used only two vertical and horizontal cross sutures for fixation of his beveled graft. For many years, however, he has used multiple sutures so that the radial sutures cross the graft margin at eight different points to hold it firmly in place (fig. 8A). Incidentally, Thomas[20] still bevels his grafts, though nearly all other surgeons are now using the nonbeveled graft. The Thomas suture and its numerous modifications, such as those of Castroviejo and Paton, are widely used throughout the world today.

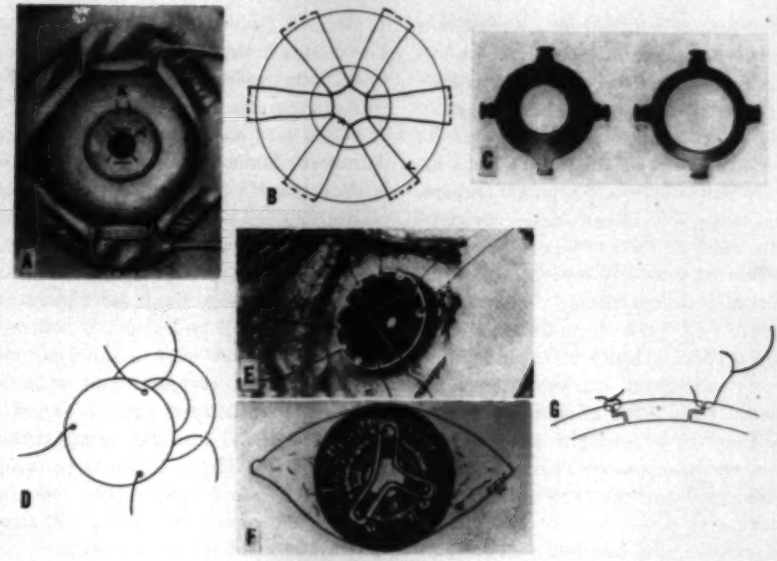


Fig. 9 (Leahey). Suture methods. (A) Wiener. (B) Lindeman. (C) Pittar. (D) Fritz. (E) Philps and Fincham. (F) Worcester. (G) Ebeling and Carrel.

Castroviejo,[34] developed his modification of the Thomas suture about 1935 (fig. 8B). Paton[45] has a further slight variation, but there are still four radial sutures so the graft margin is crossed by the supporting sutures at eight places.

Paton recently designed a plastic plate (fig. 8C), overlying the center of the graft only, to prevent cutting in of sutures. I believe this is unnecessary, as sutures can be left in for 14 days without any permanent marks. In addition, since the sutures are elevated where they cross the plate, apposition of the sutures to the graft margin is not perfect.

Bietti[46] uses two vertical and two horizontal sutures (fig. 8D). These are simple, but approximation is less satisfactory than with the eight radial sutures.

Filatov[39] for many years used sutures similar to the ones now used by Bietti; but recently (fig. 8E) he has switched to a reversed conjunctival flap anchored at the opposite limbus.

Incidentally, regular conjunctival flaps (not reversed) have been used by many surgeons, but have been universally discarded. Castroviejo[34] did his first 21 grafts using conjunctival flaps without sutures. He found this method unsatisfactory and gave it up when one of his transplants became detached. He then switched to a combination of overlying sutures and conjunctival flap with the flap actually completely covering the corneal sutures. This is the method I used in my first cases in 1937 and 1938. This method (fig. 8F) was fairly satisfactory, but it caused intense reaction in the eye. In addition, if any portion of the graft margin was not completely flush with the cornea, there was a tendency for the conjunctiva to unite to this graft margin and cause vascularization of the graft. This method was soon discarded.

Rycroft and Romanes[47] and others use similar overlying sutures, but insert a piece of egg membrane or thin rubber under them.

About 1940 Wiener[48] developed his punch technique (fig. 9A). An incision is made at the upper limbus. The flat blade of a punch is introduced into the anterior chamber, and

the corneal button punched out. I tried two of these 16 years ago, but consider both the punch technique and the suturing unsatisfactory. The cornea is stretched considerably when the bullet shaped punch engages it; and in one case one of the sutures was inadvertently pulled up into the punch and cut, causing considerable inconvenience in resuturing. In addition, the extra peripheral corneal incision may lead to anterior synechia.

Lindeman[49] developed a double "star ring" suture (fig. 9B). A continuous suture is anchored concentrically at several points on the corneal-scleral margin. Loops are left between each point of sufficient length to allow them to be brought almost to the center of the transplant. These loops are firmly connected near the center by a second ring suture.

Splints. During the past few years a number of surgeons have turned to splints to hold the graft in place.

Pittar[50] uses two plastic rings (fig. 9C). The larger ring is for marking the sites for the corneal sutures, the smaller is sutured to the cornea to cover and overlap the edge of the corneal graft.

Fritz[51] of Belgium uses a contact lens (fig. 9D) the exact size and shape of the cornea with three holes in the periphery. The lens is held by three sutures deeply placed in corneoscleral tissue at the limbus, and is left in place for 12 days. Walser[52] uses a perforated contact lens without sutures. Strampelli[53] uses sutures, but stitches a protective contact lens to the four rectus muscles. The corneal sutures may be removed through large perforations in the contact lens, which is left in place for several days after removing the sutures.

Philps and Fincham[54] use a 12-mm. contact lens (fig. 9E) with an inside curvature of 8.5 mm. radius. There are 12 tiny suture holes near the periphery. Four double-armed sutures are placed in the cornea close to the limbus, and are passed through eight of the contact lens holes and tied to hold it in place. It is left undisturbed for 14 days. The results in their series of cases were good when their grafts were photographed by the photokeratoscope of Amsler. They felt there was less astigmatic distortion in the graft than was obtained without contact lenses.

Worcester[55] developed an open molded plastic cap held by three sutures near the limbus. He also reported some very interesting research on corneal caps done under the auspices of the Eye-Bank for Sight Restoration. Plastic caps covering the cornea from limbus to limbus were sutured to rabbits' eyes, and after varied lengths of time the eyes were enucleated and sectioned. This complete corneal covering damaged the corneal nutrition. The cornea became opaque in a few days, and microscopic examination showed loss of the epithelium and considerable interstitial keratitis and iritis.

When only a partial cap was used (a six-mm. circular solid disc) the reaction was much less, but the epithelium remained absent in areas where the cap touched the cornea. When this six-mm. circular solid cap was sutured over a corneal graft, practically no union occurred at the trephine wound. Because of this Worcester decided a cap must fulfill the following requirements. (1) permit adequate respiration of both recipient and donor corneas, and (2) permit adequate support about the circumference of the wound to obtain a solid union and yet permit maximum exposure of the wound for atmospheric respiration.

Various caps were designed and tried. These varied from discs with various-sized perforations to permit respiration, to triangles with perforations. It was soon evident that another factor must be considered —namely, the circulation of fluid from the limbus to the center of the cornea. Any type of cap with a complete ring about its periphery was soon discarded and replaced by an open type. The final design—later modified for human cases—was somewhat triangular, in that it had three radiating arms,

with a large central opening (fig. 9F). Worcester reports that on the three human cases done by this method results were good, and there was less reaction to the cap than to ordinary sutures. Because of this excellent bit of research, it would seem that the increasing use of solid contact lenses as transplantation splints should be discouraged.

Vannas[18] uses a cap of condom rubber or plastic material held by peripheral sutures.

One interesting innovation is the use by Brecher and Gunther[56] of a corneoconjunctival cap taken from a cadaver. This has also been used by other surgeons, including Vannas. The second cornea is sutured loosely in place, the graft is cut and inserted, and the sutures in the corneal cap are tightened. Good results are reported, but I feel the presence of this dead tissue might predispose to infection. In addition, the work of Worcester in regard to the disadvantages of covering the graft with a solid corneal cap would presumably apply as much here as to a contact lens.

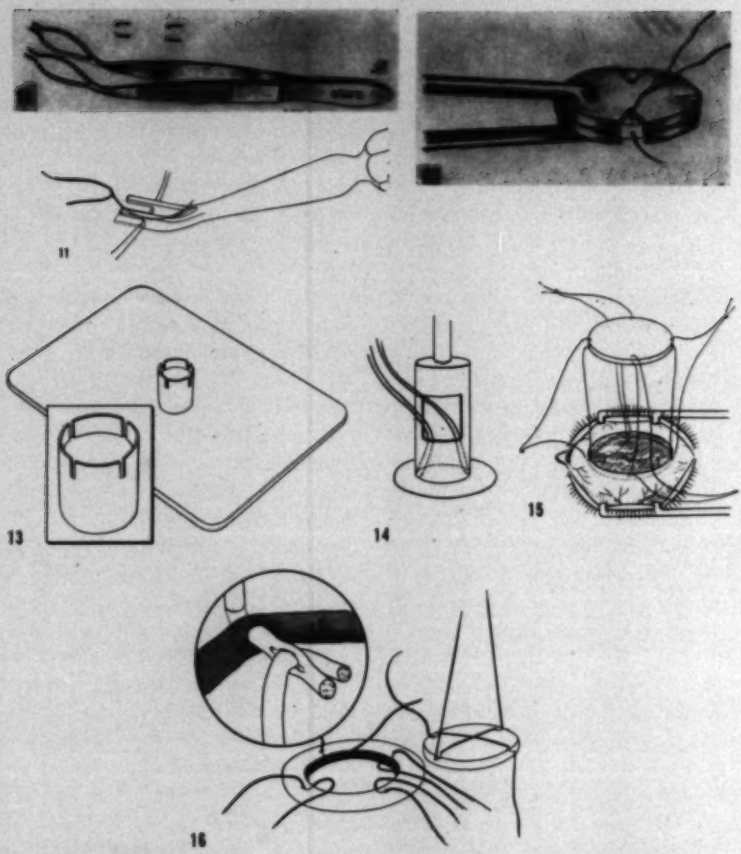
In general, I regard these plastic conformers as just a variation of overlying sutures and do not feel they possess any advantage over these sutures. These conformers are held in place by sutures to superficial tissue. Since the conformer is raised above the corneal surface, lateral push from motion of the eyeball could easily cause some of these sutures to slough out prematurely with serious consequences.

Direct sutures. During the past six years, the most worth-while change in technique has been the increasing use of direct corneal sutures. As recently as 1941 Castroviejo[34] wrote. "If the sutures are placed through any part of the graft, partial or total opacification of the latter appears." Actually, however, direct sutures had been used with limited success by Ebeling and Carrel[57] in 1921 (fig. 9G). During the early forties French surgeons began to advocate them again, and at the present time direct sutures of 6-0 silk are very widely used.

Popularity of direct sutures has been increased by two factors: (1) the need of large grafts for certain types of corneal scars, and (2) the development of special needles which cut through the cornea more easily. With overlying sutures, large grafts have always been dangerous because of a tendency for portions of the graft margins to dislocate. This could lead to loss of the anterior chamber, edema, poor union of the graft, anterior synechias, and possibly secondary glaucoma. If the area of poor union did heal, it often resulted in overgrowth of scar tissue and proliferation of connective tissue on the back of the graft.

A boon to direct sutures was the Barraquer-Greishaber needle. This had a cutting edge on the convex undersurface and passed through cornea more easily than the needles on regular atraumatic 6-0 sutures. Recently a new flat seven-mm. Greishaber needle has become available with super sharp edges on each side. This goes through cornea very easily. Since it is flat, is less difficult to handle than the triangular needle, and it is ideal for direct corneal suturing.

Graft holders. The major problem in direct suturing is inserting the first two sutures. In small grafts especially, if the free graft is held by a toothed forceps while attempting to insert the needle, it bobs around in the direction of the needle causing marked tissue distortion. Hence some means of hold ing the graft firmly while inserting the first suture is helpful. I designed and reported[58] several models of double fixation forceps one of which is illustrated in Figure 10. These are angled so that the operator's fingers do not get between his eyes and the forceps tips to obstruct his view. They have long bowed legs so that the surgeon can watch the top of the needle from above or from one side. The tips of these forceps are one mm. apart. One model is made with slightly projecting teeth for grasping the donor graft. For working on the recipient cornea lying against the lens the straight tooth



Figs. 10 to 16 (Leahey). (10) Double forceps for corneal suturing. (11) Suturing aid (Thorne and Leahey, 1950). (12) Arruga graft holder. (13) Turret-type graft holder. (14) Preplaced sutures in graft (Leahey, 1944). (15) Preplaced sutures in graft and recipient (Friede, 1938). (16) Preplaced track sutures; transfixion method (1942).

model is safer. With a projecting rat-tooth forceps, of course, there is always a possibility of scratching the lens surface. These double forceps are also excellent for repairing corneal lacerations.

A few years ago I helped Dr. Fred Thorne develop a very handy little counter pressure instrument which we called a "corneal suturing aid" (fig. 11). The original model was designed for reinserting track sutures in cataract extraction, and it was modified later for the small needles used in grafting. This instrument immobilizes the graft at, above, and below its margin, and has a tiny slot through which the needle can be passed. It is easy to use, and it is very helpful where only one or two sutures are to be put in the graft. In general it can be handled with more facility than the angled double fixation forceps.

Arruga[59] developed box forceps (fig. 12) to hold the graft while the initial sutures are placed. This has been adopted with minor variations by a number of surgeons, including Bietti and Paton.

Castroviejo recently designed a spatula-

type instrument with a round open metal box at one end with four slots in the sides. This helps to hold the larger grafts for preliminary suturing, and to lift the graft into place on the recipient eye.

In the past few years I have also designed various types of graft holders, my favorite of which is the one shown in Figure 13. Little turrets of varying size are interchangeable in this plastic base. The opening in the top of the turret is 1.5 mm. deep, and the little slots are 0.6 mm. in width. The floor of the turret (and the bottom of the slot) is elevated one quarter of an inch above the base plate to facilitate grasping the tip of the tiny needle as it is pushed through. The graft may be fixed even more firmly by stretching an ordinary rubber band over the center of the turret and around the back of the flat plexiglass base. The band is snipped with scissors when the sutures have been inserted. These graft holders are especially helpful when two or more direct sutures are used or when sutures in the graft button are being matched to tracks preplaced in the donor eye according to my method to be discussed later.

Unless a box type graft holder is used, it is good practice to leave the graft in site in the donor cornea. This aids in immobilizing the graft and also prevents trauma to its posterior surface. Katzin,[60] however, prefers to pin the graft on a piece of cork to fix it while the first sutures are inserted.

Previous techniques. Another method I originated in 1945, but later abandoned, for inserting the first two sutures in the graft is to cut almost through with a trephine, then finish cutting the button (fig. 14). This technique is satisfactory, but it is slightly more complex, and pulling on the sutures could conceivably cause more trauma to the graft margin.

Several years ago I tried passing preliminary track sutures in donor and recipient, as is done in a Verhoeff track suture cataract extraction. The idea was to cut through the preliminary sutures in both corneas, but leave the ends in place until the permanent sutures were passed. This was unsatisfactory for two reasons. The trephine often did not cut cleanly, and during subsequent manipulation the suture ends often came out.

In 1938 Friede[61] announced a very interesting technique. After cutting almost through the recipient cornea he put in four preplaced direct sutures (fig. 15). These were run from the edge of the recipient cornea to corresponding positions in the edge of the graft. The cutting of the opaque cornea was then completed, the graft merely dropped into place and the sutures tied. This technique was developed for complete penetrating grafts, but it seems equally applicable to partial ones. I tried it experimentally on animal corneas, but found the preplaced sutures got in the way; it was difficult to complete the cutting without sometimes cutting a suture, and there was apt to be needless exposure and trauma to the new graft.

Anyone using Verhoeff track sutures for cataract extractions finds that the final 6-0 suture often actually transfixes the preliminary track suture.

As a matter of fact Verhoeff[62] had once suggested utilizing this ability to put one suture through the other for re-inserting cataract sutures. In 1942, it was suggested by Cogan and Sullivan[63] that this technique might be adapted for preplaced transplant sutures. Consequently, I experimented with a technique combining the Friede method, preliminary track sutures, and this Verhoeff idea.

Track sutures were inserted in the recipient cornea. After cutting through the sutures and almost through the cornea, new sutures were put through the tracks as in the Friede technique and the needles removed. Cutting of the opaque button was then completed but left in place temporarily. The donor graft was cut and four sutures inserted in it corresponding to those in the recipient (fig. 16).

The central end of each suture in the recipient cornea was laid on a small rubber

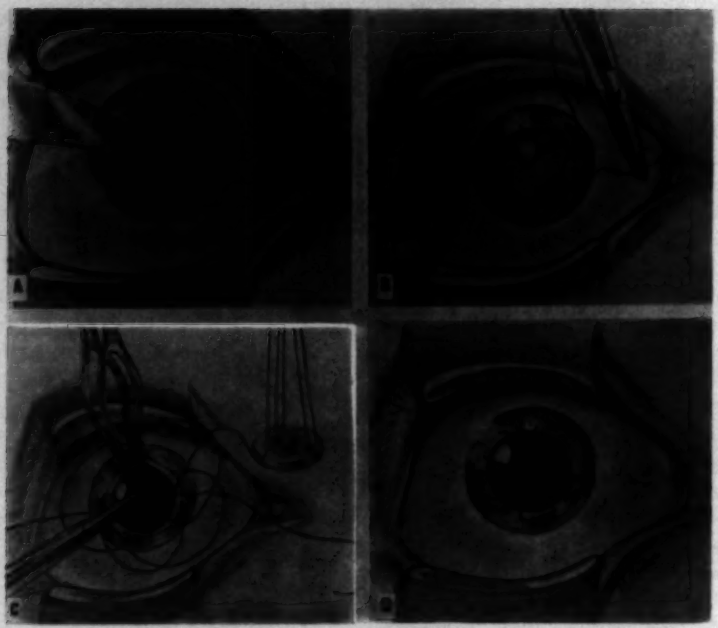


Fig. 17 (Leahey). Use of preliminary stained track sutures (Leahey, 1948). (A) Plastic markers notched at desired points indicate identical suture sites on donor and recipient. (B) Preliminary sutures stained with methylene blue are inserted at identical sites in donor and recipient and pulled through, leaving blue tracks. (C) Overlying sutures have been inserted. Cutting of opaque cornea is completed and new graft with sutures already inserted is swung into place. Sutures in graft are passed through tracks in recipient. (D) Direct sutures are tied first; overlying sutures are then pulled through and tied.

mat, the needle from the equivalent graft suture speared through it, and the needle cut off. By pulling the transfixed thread in the recipient cornea it was possible to pull the graft suture through the track in the recipient also. Each graft suture was pulled through in this manner and tied to complete the operation.

This technique was rather complicated, slow, and difficult; and sometimes the transfixed suture pulled out. Because of this, and since direct sutures at that time were considered of dubious value, the method was abandoned without being tried on human eyes.

In 1954 Avello[64] revived Friede's preplaced sutures for partial penetrating transplantation, but reported the method erroneously as an original technique.

In 1948, I reported the use of preliminary track sutures[65] stained with methylene blue. If more than one direct suture is desired, perfect apposition of sutures preplaced in both donor and host is possible only by using a marking device. For this purpose I designed markers made of transparent plastic notched at the suture sites (fig. 17A). The preliminary track sutures stained with methylene blue are inserted at the desired places on the recipient cornea after marking the graft area with the trephine (fig. 17B). The track runs one mm. on each side of the trephine cut. The sutures are pulled completely through, leaving blue tracks. This process is repeated on the donor cornea. The usual overlying sutures are also inserted in the recipient cornea.

After the donor graft is cut, new sutures are inserted in the blue tracks of the donor graft. For these sutures I utilize one of my

three special instruments, the double fixation forceps, the corneal suturing aid, or the turret type graft holder. The graft is lifted into its new position and the same sutures are passed through the blue tracks of the recipient cornea with the aid of the special double forceps (fig. 17C). The direct corneal sutures are tied first. If overlying sutures are also being used, they are pulled through and tied (fig. 17D); otherwise additional direct sutures are inserted. These later direct sutures are much easier to insert as the graft has now been immobilized, markedly simplifying passage of the needles.

This effective but rather cumbersome technique was used extensively several years ago before corneal needles such as those of Greishaber were available. With these very sharp needles it is relatively simple to insert sutures in the recipient cornea without undue tissue manipulation and trauma. Another factor to be considered is that even with careful marking technique the tracks in the new graft and in the recipient cornea often do not match exactly.

Present technique. Because of these factors, I now put only two preliminary stained track sutures in the recipient cornea. Because of the ease with which sutures may be inserted in the graft with the plastic turret graft holder, stained track sutures in the donor are omitted completely. With the graft held firmly in the holder, two to four sutures are easily inserted in the donor cornea without need of these tracks.

Regardless of how the initial sutures are inserted in the graft, I like to use a single double-arm suture for two opposing suture points. This eliminates many extra threads and loose ends. Where multiple sutures are desired, the same method is used.

The suture ends in the new graft are cut to approximately two-inch lengths. The turret graft holder with the graft still in place is held close to the recipient eye with the ends of the sutures lying on the turret base plate (fig. 18A). The two ends of one suture are bent back upon themselves and picked up with smooth forceps, so that the graft is suspended in the middle and the needles are locked on each end (fig. 18B). The assistant lifts off the scarred corneal button and the new cornea is dropped into place. After the two needles on the opposing ends of one suture have been carried through the blue tracks in the recipient cornea, a blunt iris hook is inserted under the center of the suture to bring it up in a loop two cm. long (fig. 18C). This central loop is then cut, and the first two sutures are tied with the smooth forceps.

If four preliminary sutures are inserted with the turret holder, precautions must be taken to avoid dropping off the seven-mm. Greishaber needles the two sutures not held by forceps. The ends of the second two sutures should be blocked with tiny silver artery clips or knots before lifting the graft into place. After inserting the first two sutures through the preliminary stained tracks, the knot or artery clip is cut off the end of the third suture which is then passed through the recipient cornea with the aid of sharp-toothed forceps (fig. 18D). The corneal margin is everted slightly to increase visibility and reduce danger of trauma to the lens and the suture is readily inserted from the cut edge to the periphery. The fourth suture is then similarly inserted.

Handling of the fine sutures, pulling them through, and tying the knots are greatly facilitated by the use of two narrow smooth McCullough utility forceps with cross serrated jaws. With two forceps the knots can be tied more quickly and under more accurate control than by more customary methods. If overlying sutures are also being used they were, of course, preplaced before completing the trephining. These are now pulled through and tied (fig. 18E). Otherwise additional direct sutures are inserted.

As mentioned previously, I have preferred grafts 4.5 or 5.0 mm. in diameter, with the great majority in this series being 5.0 mm. Except for early conjunctival flap cases, all of the 4.5-mm. grafts and most of the early

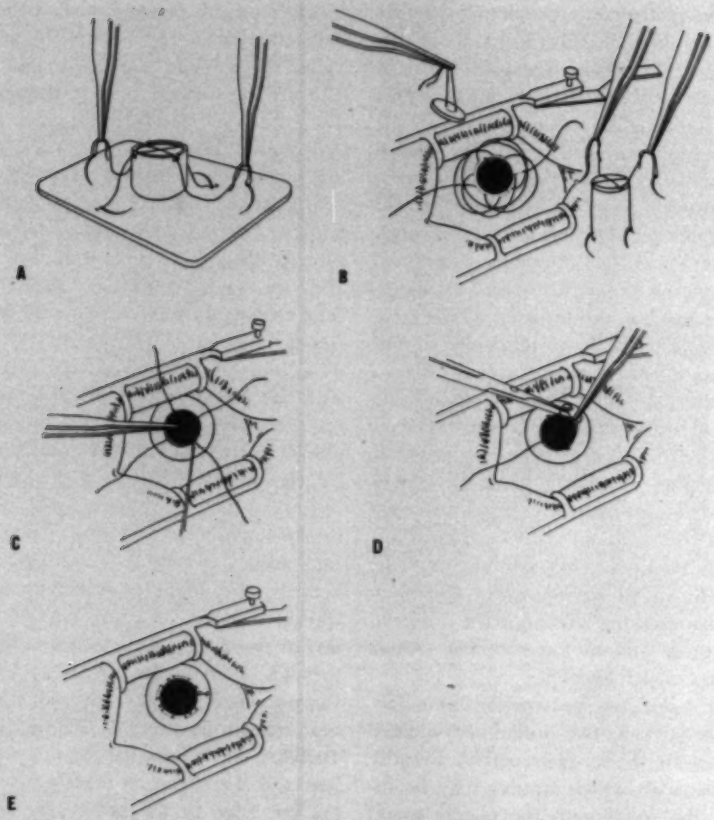


Fig. 18 (Leahey). Use of preplaced sutures in graft and preplaced blue tracks in recipient (Leahey, 1951). (A) Sutures inserted in graft held in turret holder; two ends of one suture doubled back on themselves so forceps will hold needles in place; ends of other sutures blocked with silver artery clips or knots. (B) Assistant lifts out old cornea; with two smooth forceps, graft is lifted into position by opposite ends of one suture. (C) The two ends of one suture have been carried through blue preplaced tracks. Before tying, center of this suture is pulled up in loop with aid of iris hook and cut. (D) First two sutures have been tied. Grieshaber needle on third is being passed through recipient with aid of sharp-toothed forceps. (E) Four direct sutures have been tied.

5.0-mm. ones have been held in place only by the overlying sutures of Castroviejo. In about one third of the 5.0-mm. grafts (including *all* of my recent ones) one or two direct sutures have also been used. Since at least one or two direct sutures are now used in every transplant and since satisfactory suturing of a graft of only 4.5 mm. is difficult, I have discontinued use of 4.5-mm. grafts in recent years. In 5.5- to 6.0-mm. grafts, overlying stitches are combined with two to four direct sutures. In grafts 7.0 mm. or more, overlying sutures are omitted completely and the transplant is held in place by 10 to 22 direct sutures.

There were no aphakic cases in this series, but, in general, grafts in aphakia are a poor risk and require special consideration. Numerous direct sutures are the rule, and before trephining most surgeons insert a wide spatula across the anterior chamber behind the graft area to prevent massive vitreous

loss. Besides the danger of excessive vitreous loss during operation, there is a tendency for vitreous to get between the wound margins and delay healing. In one aphakic case done by another surgeon a few years ago the patient squeezed violently when the stitches were being removed on the 12th day, and the apparently successful graft popped up in the air. This eye was later enucleated.

Total penetrating keratoplasty. Recently there has been a revival of interest in total penetrating keratoplasty. Since 1913, when Filatov published his first attempt, this had been tried by a great many surgeons without success. The most interesting early contribution was the previously described technique of Friede[61] used between 1935 and 1938. All of his cases were failures, so he concluded along with the other authors that successful total transplantation could not be done.

Until 1950 the literature was almost as discouraging as earlier reports. DeJean[66] was so disappointed in the results of total grafts that he turned to subtotal grafts, meeting with more success. LeGrand,[67] in one case out of 11, was able to get useful vision following a secondary partial penetrating graft. Thomas, Cordier, and Algan[68] obtained 20/200 vision in one case. Sommer[69] included a fringe of conjunctiva in his grafts; all were soon opaque. Cavka[70] reported six cases which became totally opaque within three weeks. Castroviejo,[71] however, reported 21 cases, in 12 of which there was considerable improvement in vision lasting up to 10 months at the time of his report (1950).

His technique included removal of the lens when necessary, extensive removal of iris, fixation with about 22 direct sutures, and injection of air at the end of the operation. It is probable that the air injection was the greatest single reason for this radical and abrupt improvement in results.

Despite this encouraging report complete penetrating keratoplasty must still be regarded as a very speculative operation of poor prognosis, and should be considered only when there is complete degeneration of the entire cornea.

Fibrin fixation. Recently fibrin has been suggested as a substitute for sutures. In 1946 Brown and Nantz[72] showed experimentally that fibrin increases the adhesive power of a corneal wound. In 1950 Tassman[73] advocated the use of fibrin to seal corneal grafts. He and other surgeons have done cataract extractions and also a number of grafts successfully by this method. In sections of dogs' eyes in which the fibrin coagulum was employed, not only did they find "no downgrowth of epithelium into the wound, but in all cases there was definite evidence of increased proliferation of fibroblasts in a shorter period of time than was found in the control eyes." Tassman reported three successful penetrating grafts kept in place by this technique without the aid of sutures. The technique is simple, and he considers it very effective.

Dunnington and Regan,[74] however, have done a memorable piece of research on the effect of sutures and of thrombin upon ocular wound healing, and they are less encouraging about the fibrin fixation. They studied fibrin fixation of cataract incisions in monkeys. After adding the plasma, they held the edges of the wound together for about one minute. No sutures were employed.

Histologic examination at the end of two days showed fibrin deposits beneath the conjunctiva in cases in which a flap was used. Irrespective of the use of a flap, fibrin was present between the wound edges, producing poor approximation. There was no evidence of fibroblastic proliferation, and in some instances epithelium was seen growing down between the tips of the wound. At the end of four days some fibroblasts were seen in the vicinity of the incision, there was little or no round cell infiltration, and the epithelium had proliferated still further along the wound. When a conjunctival flap was present, the fibrin and subepithelial tissues constituted a large anterior plug. At the end of one week fibroblasts had infiltrated this subepithelial tissue and invaded the fibrinous meshwork, making a broad scar which extended throughout the entire wound. When a corneal incision was used, the epithelial downgrowth sometimes lined both edges of the wound throughout its entire length. Fibro-

blasts were present beneath the epithelium. After two weeks, all incisions seemed well healed with dense broad fibrous cicatrices, the only exception being in those eyes in which the edges of the corneal wound were epithelized.

From these studies we believe that in the presence of fibrin normal healing will occur without the round cell invasion of necrosis found in the vicinity of sutures. During the first few days of healing, fibrin tends to separate the edges of the wound. This may produce three undesirable effects:

1. The cohesive action of properly approximated wound edges is lacking.

2. A broad fibrous cicatrix will be created, which although usually satisfactory will lack the tensile strength of normal tissue.

3. As suggested by Brown and Nantz, in the presence of a corneal incision epithelium may proliferate along the lips of the wound, producing a weakened area or possibly epithelization of the anterior chamber.

They conclude that since thrombin prevents apposition of the wound surfaces and is of very limited tensile strength, it is not the ideal material to insure accurate closure of ocular wounds.

We have had no experience with this method in the Boston area, but because of this research it is probable that the method will not become widely used until many more cases have been reported. Since penetrating grafts can be dislocated by lid squeezing, sutures appear to be a safer method on active patients. In the case of the lamellar grafts, however, adhesive quality is desired rather than tensile strength; there is little danger of dislocation by simple squeezing, as when vomiting, so in these grafts it is possible that fibrin fixation may become the method of choice. In such event the operation certainly would be much simplified.

At the present time Tassman[75] is still enthusiastic about this method. He reports that several men are using it for corneal lacerations and ulcerations, but to his knowledge no one else is using the technique for grafts. He now agrees, however, that sutures are also desirable to insure fixation.

Removal of sutures. During the 1930s, overlying sutures were routinely removed in six days, as it was thought they would cut into the cornea leaving permanent marks, or become infected. Removal of sutures at this early date is difficult, dangerous, and unnecessary. Overlying sutures are now removed in 12 days. If one edge of the graft has been partially dislocated, they have been left in up to 18 days. After 10 days these cross sutures usually leave a slight mark in the graft surface. Only the epithelium seems to be damaged, however, and two days later these marks have routinely disappeared in my cases. Direct sutures are left in 18 days, and, if the patient is unco-operative, as much as a week longer, without apparent damage.

Direct sutures are considerably more difficult to remove. Some surgeons[12] use a sharp knife or discission needle. I prefer curved, sharp-tipped iris scissors. In most cases, the suture is cut before it is grasped by the forceps. When removing the direct sutures, it is important to pull from the recipient side and not from the graft side to prevent possible gaping of a poorly healed wound.

When stitches are removed on the 12th day, one nurse holds the lids open and a second holds a focused flashlight. These small "pen lights" give adequate illumination and do not cause the photophobia or squeezing associated with regular operating room lights. When the direct sutures are taken out on the 18th day, such careful precautions are not necessary and an ordinary ophthalmic spotlight is equally satisfactory. Rarely has it been necessary to bring an especially nervous patient to the operating room and use sodium pentothal anesthesia in order to remove the transplant sutures safely.

Use of air in anterior chamber. Undoubtedly the greatest single improvement in my technique in recent years was the use of air injections in the anterior chamber postoperatively. I began to do this in 1945. After the sutures have been tied and the graft edges patted down into perfect position, the tip of a Randolph cyclodialysis cannula is gently inserted in the incision for about 0.5

mm. perpendicular to the lens surface, and a moderate sized air bubble is injected. This air bubble balloons the anterior chamber up, and remains there much better than saline solution. It takes three days to absorb and usually prevents what was formerly the most common complication, anterior synechia. To minimize further the danger of anterior synechia, adrenalin is injected subconjunctivally at the end of operation, and two drops of four-percent atropine solution are instilled in the conjunctival sac.

In one recent case, the eye was so extremely soft that it was impossible to trephine safely. In this case a very oblique incision was made through cornea near the limbus with a Graefe knife after the manner described by Chandler.[76] Air was then inserted with a 26-gauge, medium-bevel needle to make the eye firm. The obliquity of the corneal incision left a self-sealing wound, so the operation was easily completed. After the graft was in place and suturing was completed, another air bubble was easily inserted through this peripheral knife incision (much more easily than through the regular graft incision). This method is not to be recommended routinely, however, as in some cases the knife incision may not remain self-sealing when the cornea is pressed in by the trephine; in this case the operation might have to be temporarily abandoned.

Complications

Unfortunately, complications are frequently encountered.

Dislocation of the graft

I have never seen a completely dislocated penetrating graft, but many have been reported and probably many more have been studiously forgotten. It was of course much more common in earlier days. Elschnig[77] reported expulsion of the graft in one sixth of his cases! This is a catastrophe, but rare cases have been saved by immediately replacing the graft or putting in a new one. In one such case in Philadelphia, several years ago, the new graft was found on the dressing the first time it was changed. No corneas were available through regular channels; but, because of the emergency, permission was secured to take a cornea from a corpse which had been dead for many hours in a local morgue. The second graft held satisfactorily and the eye was saved.

Loss of the graft into the anterior chamber is even more rare, since the graft rests at first upon the lens, and is elevated by the pressure of the aqueous only after the wound is sealed.

Slight elevation of one section of the graft is much more common. In earlier years, when square grafts with beveled edges were used without any direct sutures, this partial dislocation was more common and was treated by covering with a conjunctival flap. The five cases so treated in my series healed, but in each case the graft vascularized with little visual result.

At the present time this bulging of the graft margin, either general or in one quadrant, is much less frequent due to improved techniques and suturing. If the graft is poorly united or protrudes above the rest of the cornea over any considerable area, moderate pressure with an Ace elastic bandage is applied as a complete head bandage amply supported with adhesive tape so that it will remain in place for seven to 10 days. If the dressing is changed every day or two, and the eye is opened each time, this bulging or herniation can recur at each dressing with little ultimate improvement. With continued pressure, these elevated graft edges nearly always flatten out. When bulging is slight, a simple Elastoplast eye pressure dressing often suffices without the head bandage.

If there has been much elevation of the edges with or without gaping, the prognosis is poor for a clear graft, due to the tendency for connective tissue to proliferate from this area over the back of the graft (fig. 19). Since the cornea will usually heal solidly, however, a regraft can be done later if desired.

Fig. 19 (Leahey). Permanently opaque corneal margin following poor approximation of sector and elevation of graft edge.

Anterior synechias

Of all postoperative complications anterior synechias formerly were the most common. They are more apt to occur with very large grafts, or if the cornea is very thin with consequently less exact approximation. Delayed reformation of the anterior chamber or subsequent leaking of the wound is usually the causative factor.

The use of air injections in the anterior chamber at the end of operation has helped to reduce the incidence of anterior synechias in my own series to a fraction of its earlier frequency. Frequently the air bubble cannot be retained in the anterior chamber. In these cases, every two days wide dilation of the pupil is insured, at least temporarily, by two drops of four-percent atropine and four drops of 10-percent Neosynephrine. To avoid dislodging the graft the patient is directed to look up, so the graft is covered and supported by the upper lid. The lower lid is gently pulled down and the drops instilled in the lower cul-de-sac.

Slight anterior synechias at the edge of a clear graft are almost certain to cause clouding of the graft in a few months. They may cause proliferation of connective tissue on the back of the graft, or they may cause haziness in the stroma or edema of the epithelium. They also may cause glaucoma. Occasional patients have shown synechias for many years without complications, but since it is impossible to know exactly which eyes will not be harmfully affected, an attempt should always be made to remove these adhesions. Lysis of the adhesions was necessary in 20 percent of the grafts done since 1944.

In 1941[78] and again in 1947[79] I reported methods of freeing these synechias through a cyclodialysis opening made four mm. outside the limbus (fig. 20A). The spatula is slid into the anterior chamber (fig. 20B), the synechia is swept away, and air is injected through a cyclodialysis cannula (fig. 20C). The air bubble usually prevents hemorrhage into the anterior chamber as well as a reformation of adhesions. The scleral incision is made closer to the limbus than for a regular cyclodialysis so the spatula can sweep far into the anterior chamber with less danger of pressure on the edge of the lens and also with less disturbance to the angle of the iris. Essentially similar methods have been developed independently by Castroviejo and by Barraquer,[81] and recently Castroviejo[80]

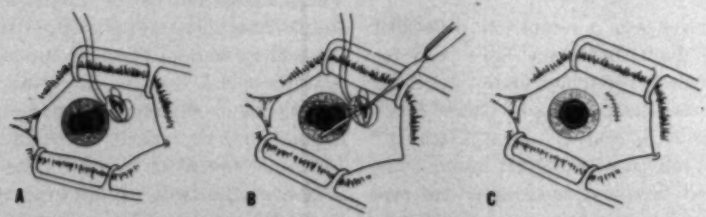


Fig. 20 (Leahey). Lysis of anterior synechia. (A) Cyclodialysis incision four mm. from limbus, one central scleral-conjunctival suture inserted. (B) Sweeping away synechia with Elschnig spatula. (C) Air bubble has been inserted and deep suture tied.

designed a hollow cyclodialysis spatula so that adhesions could be freed and air injected through the same instrument.

In some cases of extensive old anterior synechias, sweeping motion with a dull spatula will tear the iris off at the limbus rather than at the adhesion site. For these cases, cyclodialysis spatulas with blunt tips and sharp edges are effective.

Glaucoma

This is one of the worst complications and, unfortunately, in my experience one of the most common. In this series, 33 percent of cases had increased tension at some time during convalescence. Glaucoma is much more frequent if the iris and ciliary body have participated in some fashion with the original corneal disease, mainly because the angle of the anterior chamber has been partially blocked by previous cellular debris or old peripheral anterior synechias. In this series glaucoma has been much more frequent in eyes with old chemical burns, disciform keratitis, and interstitial keratitis, and uncommon in the familial dystrophy and keratoconus patients (table 8).

Glaucoma is to be expected in cases with marked anterior synechias, but it also occurs in eyes with apparently perfect grafts and no visible adhesions. Many of the early glaucoma attacks are of mechanical origin due mainly to prolonged dilatation of the pupil with angle closure, and respond immediately to intensive treatment with miotics. Excellent results are obtained with four-percent pilocarpine plus a solution of 1.5-percent Carcholine in 1/3,000 Zephiran. Because of the danger of this angle-closure glaucoma, atropine is usually discontinued two weeks after operation even though ciliary injection and light sensitivity are usually present for several more weeks. Except in the few cases with high tension starting suddenly three to five weeks after transplantation, glaucoma is seldom of the acute type.

If the graft is reasonably clear, it is often possible to inspect the angle of the anterior chamber by gonioscopy and determine the type of surgery to be done. In most cases the angle will be found to be blocked either from previous iridocyclitis or from a prolonged flat anterior chamber. Cyclodialysis was for many years my most common remedial operation, but I used trephining with success in two early cases. For the past five years I have employed perforating cyclodiathermy almost exclusively. A 1.5-mm. needle is inserted through conjunctiva and sclera five to eight mm. from the limbus, in eight to 10 places. In most cases the patient was allowed to go home the same day; but the procedure frequently had to be repeated on one to three subsequent occasions.

Injury to the lens

One traumatic cataract occurred in this series but was recognized only during convalescence. It was probably caused by the keratome tip during the excision of a square graft. Many such cases have been reported in the literature. If recognized at the time of operation it is considered wise to complete the capsulotomy and remove the nucleus before tying the graft sutures. In the case of large grafts there also have been reports of a number of cases of dislocation of the lens.

Vascularization

Vascularization is far more common if the eye remains irritable for a considerable period or if there have previously been blood vessels in the recipient cornea. Interstitial keratitis cases are especially apt to show marked new vascularization. About 10 days after operation three of my cases showed new typical interstitial keratitis involving the recipient cornea, with countless small vessels opening up and growing toward the graft. For a few days there may be a circle of vascularity surrounding the graft, and then the graft is also invaded by countless deep radial vessels. Soon both the new graft and the recipient cornea may resemble the vascularized "salmon patch" characteristic of the second stage of interstitial keratitis.

Vascularization of the graft may often be controlled by beta radiation but it is usually not practicable or safe to insert a speculum in the eye to administer beta rays for three to four weeks following transplantation.

In cases with a flare-up of old interstitial keratitis, the treatment of choice is steroids given orally. In two cases this was started when the condition was first recognized, between the 10th and 14th days, and improvement was dramatic. After the 14th day the steroids were also given locally. Three recent interstitial keratitis cases were given Meticorten beginning five days after operation. This apparently caused no interference in graft healing, and there was no flare-up of the keratitis.

Proliferation of tissue on posterior surface of graft

Proliferation of connective tissue on the back of the graft is not uncommon. This is practically sure to occur in the presence of anterior synechias. In other cases it grows in from fibroblastic tissue at the margin of a perfect graft (fig. 21). There is no effective treatment for this, as radiation is apparently not of much use. Fortunately, in many cases proliferation occurs only one mm. or so on the posterior surface and then stops, but in other cases the fibroblasts grow entirely across the graft leaving a new layer of connective tissue behind Descemet's membrane.

About half of the cases with this posterior connective tissue proliferation showed slight edema of the corneal stroma and epithelium in the area immediately overlying the proliferation.

Approximately 26 percent of my cases in this series have at least a one-mm. area of connective tissue proliferation posteriorly somewhere on the graft margin. In 10 percent of the series this was enough to lower the acuity of otherwise successful grafts to less than 20/70, with the final acuity of most of this impaired group varying from 8/200 to 20/200.

In another eight percent with serious complications such as prolonged elevation of graft margins, extensive anterior synechia, or long continued inflammation, the connective tissue formed a complete or almost complete membrane over the posterior surface of the graft.

When the membrane is complete, Lohlein[82] has advocated making a keratome incision and pulling the membrane off with a blunt iris hook. This would be a difficult procedure when the anterior chamber is collapsed, with danger of injury to the lens. It is probable a new graft would be a lesser insult to the eye.

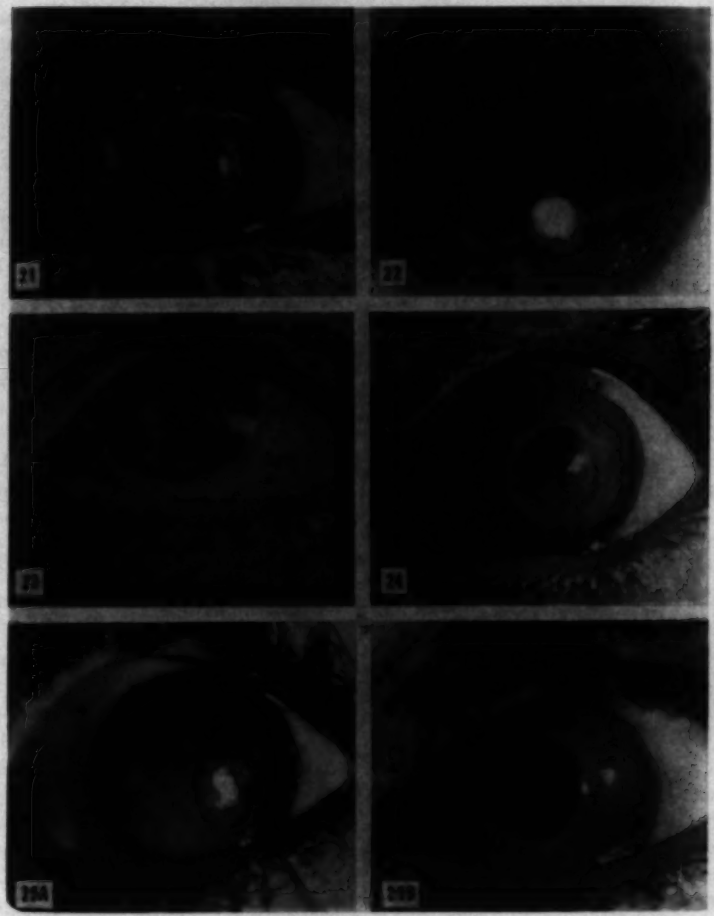
It is also possible to have proliferation of epithelium on the back of the graft as a result of a poorly approximated wound or the introduction of epithelial tissue at the time of trephination. The one probable case in my series is shown in Figure 22; long fingers of new cells reach well across the posterior surface of the graft.

Iris pigment can also proliferate on the back of the graft. Theoretically, donor pigment could be implanted with the graft, but in this series the nine percent with visible pigment all acquired it from anterior synechias which were freed. In only two cases did the pigment proliferate. In these eyes (fig. 23) the pigmented areas grew for two to three years; but after four and six years, respectively, further growth has not been evident. Vision was not adversely affected.

Edema of the graft

This is another complication which is both common and serious, and for which there is no really effective therapy, provided it is not the result of anterior synechia or glaucoma.

In some cases the customary edema found the first two weeks after operation may remain stationary or gradually increase (fig. 24). In others, the graft may appear quite clear after about three weeks and then suddenly develop slight edema. This gradually becomes worse and in a few weeks or months there may be actual bullous keratitis.



Figs. 21 to 25 (Leahey). (21) Proliferation of connective tissue over square graft. Growth stopped within six months and graft remained as pictured for eight years. (22) Probably epithelial proliferation on back of graft. Growth stopped within about six months and has remained as pictured for four years. (23) Pigment proliferation on back of cornea after freeing of anterior synechia. Slight growth for three years, no change for past two years. (24) Edema of cornea following apparent success. Still present two years after grafting. (25) Late edema of cornea. (A) Edema of cornea from injury; extensive rupture of Descemet's membrane. (B) The same eye 10 months after clear graft. Permanent edema developed suddenly after 13 months.

When bullas are present there is usually an associated slight irritation and occasionally a tendency to eventual partial vascularization.

This edema of the graft occurring about three weeks after operation has been widely discussed. Klima[83] produced an allergic inflammatory reaction in rabbits' corneas by repeated injections of corneal extract into the stroma. He thinks the graft causes an allergic reaction in the host cornea owing to a group specific difference between them which leads to disease of the graft. In 1951 Maumenee[84] reported a series of rabbit experiments showing that donor-recipient sensitivity can be brought about and that it can

cause opacification of the graft. He induced this sensitization by supplemental transplantation of skin from the same donor to the recipient's abdomen.

This tissue sensitivity is undoubtedly the cause for some opaque grafts, but in my own series this type of case occupies a relatively unimportant percentage (about five percent). In most of my cloudy grafts the slight edema present after surgery merely persisted and became worse.

In a few cases (four percent) grafts were apparently perfectly clear with no complications for 10 to 15 months and then suddenly developed marked edema within a period of a few days. This very late edema should presumably not be regarded as of allergic origin. In all of these late cases grafts had been set in corneas severely damaged by previous inflammation. Severe lime burns were the worst offenders, but in two of these late cases the eyes had been severely damaged by very extensive former disciform keratitis. In another case there was almost complete edema and deterioration of the cornea due to a blow by a stone 12 years previously with rupture of Descemet's membrane (fig. 25A). At the time of transplant a shred of Descemet's membrane was running across the lens surface from the 10-o'clock to 4-o'clock positions, indicating corneal damage well beyond the limits of the new graft. This graft was also sparkling clear for 13 months with the shred of Descemet's membrane easily visible (fig. 25B). The cornea then became edematous within a two-day period, assuming an appearance exactly like that of the host cornea. In another case with a complete leucoma of the cornea from a lime burn, the graft was completely clear for six years, but during the next five years developed progressive faint edema of the graft stroma.

Since edema of both early and late type is much more common in previously damaged corneas than in cases with keratoconus or familial dystrophy, it is probable that the importance of the antigen factor, while considerable, is generally overestimated.

The thickness of the graft may also be a factor in edema. Welter[80] has stated that the thickness of the graft varies from 0.74 mm. to 1.03 mm., while that of the scarred cornea varies from 0.55 mm. to 2.67 mm. When the graft is thinner than the recipient there is relatively little disadvantage. When the graft is thicker it projects not posteriorly but anteriorly, probably because of pressure of the aqueous on the back of the graft as soon as the chamber is reformed. This forward bulging of the graft causes the corneal stroma at the margin to absorb tear fluid and swell further. This bulging also allows epithelium to grow over part of the cut section and thus oppose normal repair.

Infection

Infection is fortunately an extremely rare occurrence. In many contemporary series there have been no infections. There was one panophthalmitis in this series 11 years ago. The donor eye had been removed in a distant hospital by a person with no ophthalmic experience. It was not cultured or washed carefully, and it is probable infection was introduced directly with the graft. Since then all donor eyes have been washed in three successive cups of saline just before the graft was cut, and penicillin has been given for five days after operation as an extra precaution.

Recurrence of the original corneal pathology

The consensus at present is that the graft preserves its own identity but is gradually paritally replaced by the tissue of the host. It is reasonable, therefore, to expect that the graft would take on many of the qualities of the host cornea in the course of time. Recurrence of interstitial keratitis has already been discussed. Paufique describes recurrence of tuberculous keratitis in the graft, and I have observed cases with lipoid dys-

trophy develop similar fatty changes in the portion of the graft adjacent to the diseased host tissue. Corneal edema from any cause is notorious for its recurrences. Recently I observed recurrence of dendritic keratitis in two grafts which had been clear for two and four years respectively.

Authors vary widely in regard to recurrence of the hereditary dystrophies. My series indicates that if the dystrophy is of a progressive type such as Groenouw's nodular dystrophy or lattice keratitis, the graft will ultimately again acquire this disease. The graft, however, will acquire the pathology probably at the same rate of speed as the original cornea developed it. My 19-year series includes 25 cases of nodular dystrophy and lattice keratitis and for nine years none of these showed any evidence of recurrence. After nine years, however, in one case, and 11 years in another, definite beginning recurrence of lattice keratitis was discovered. Recently a recurrence in seven years was also found. Nodular dystrophy recurrence has not yet been seen in this series, nor am I aware of its having been reported elsewhere.

There have been reports in the literature of a few cases of early to moderate Fuchs's dystrophy improved by grafting.[86, 90] Since completing this series, I did an eight-mm. perforating graft in a Fuchs's dystrophy case, and followed it up five months later with an intracapsular cataract extraction via a deep scleral section. This cornea is still clear four months later. Since in the past, however, all types of edema of the cornea have been especially prone to recurrence, I believe that many of these apparently successful cases may again become cloudy in a relatively short time.

There has yet been no case in the literature of recurrence of keratoconus. This is probably because most keratoconus operations are on adults. It may be assumed the disease should take 10 or 15 years to appear again. The patient would by that time be outside of the age group of increasing keratoconus, so for this reason there actually might be no recurrence.

Refractive error

A minor complication often found is a large refractive error. Myopia is frequent and often increases within the first four months after operation probably due to contraction of the scar tissue ring around the graft. Considerable astigmatism is also usually present, with the small grafts in general showing more astigmatism than large ones. In this series there were a number of cases in which there was nearly normal acuity with two to seven diopters of astigmatism. One woman with a transplant followed by a cataract extraction obtains 20/35 vision and reads J1 print with a +4.5D. sph. combined with a −12.0D. cyl. Undoubtedly, these patients could get 20/20 vision with contact lenses, but I have not yet ordered one for a transplant case.

In all types of corneal grafts the oral use of Meticorten starting eight to 10 days after operation and the topical use of Hydrocortone solution starting two weeks after operation has proven of great value in preventing complications. Cortisone reduces inflammation and by so doing lessens the tendency for grafts to vascularize and for connective tissue to proliferate over the posterior surface. Both by decreasing iridocyclitis and by shortening actual atropinization time, cortisone also decreases the percentage of postoperative glaucoma. By decreasing allergic reaction it is probable that it also helps decrease the tendency toward edema in many cases.

Results

Results are meaningless without consideration of the type of cases. Complete statistics appear unfavorable since the operation is done on many nearly hopeless eyes and on eyes having many other defects. The gradual but steady improvement in results,

however, has paralleled that of separated retina repair and has been truly gratifying. In Filatov's 1924 series 15 percent of the grafts remained clear.[87] By 1933 his percentage of clear grafts had increased to 29 percent. Tudor Thomas[88] in 1936 reported 28 percent clear. In 1947 the American Academy symposium[89] reported 36.5 percent remained clear. In the "favorable groups," however, 68.3 percent of the grafts were clear. The 1948 report of the cases of Paufique, Sourdille, Offret, and Franceschetti[40] lists 36 percent clear and 48 percent with visual improvement. By 1950 Paton[90] had done 100 cases with 55 percent remaining clear. Of his 23 grafts in the "most favorable group," however, 82.7 percent were clear.

By his 1954 report,[91] Paton's percentage of clear grafts (this series also includes many lamellar grafts) had climbed to 64.5 percent. As Paton himself mentioned, this figure is misleading on the high side for two reasons. Thirty-nine percent of all his grafts were in keratoconus eyes, and when multiple grafts were done on the same eye, only the clarity after the final operation was included in the statistics. This eliminated many unsatisfactory results. In 1955 Fine[92] reported 74 percent improved. His series also included 39 percent keratoconus cases.

The true present value of any operation should be based on statistics of the current technique rather than on those of previous inferior operations. At the present time, transplant results of practically all surgeons are very much better than those of a few years ago.

By discarding the results of earlier years, it is possible to get a more accurate appraisal of present value. In the following statistical summary, operations done during the first years of my series starting in 1937 have been omitted and only a more recent group of 100 consecutive cases has been included. These were done between 1944 and 1954 and include 91 primary grafts and nine regrafts. No case done during this period has been omitted, and all have been followed for at least one year.

TABLE 1

SUMMARY OF PREOPERATIVE VISUAL ACUITIES OF 100 CONSECUTIVE TRANSPLANT PATIENTS

30 eyes	Light projection
27 eyes	1/200 to 2/200
37 eyes	3/200 to 10/200
5 eyes	11/200 to 19/20
1 eye	20/200

In evaluating this series, it is well to bear in mind that the average original visual acuity was extraordinarily low due to the extreme pathology in cases selected for operation. In the 100 consecutive cases in the appendix, 57 eyes had preoperative vision of 2/200 or less (30 eyes, light projection only; 27 eyes, 1/200 or 2/200); 37 eyes had 3/200 to 10/200; five eyes had 11/200 to 18/200; one eye had 20/200. In other words 94 percent of all eyes selected for operation had original vision of 10/200 or less and only one percent had better than 18/200 acuity (table 1).

Standards for judging results vary widely. In this series "improved" means that the postoperative visual acuity is at least 10/200 and also is at least three times the preoperative acuity expressed in percent; that is, an initial vision of nine percent (18/200) must have improved to 27 percent (20/70).

As in Fine's series,[92] an exception is made in cases with original vision of light projection only. For these unhappy people he felt vision of only 1/200 represented a distinct improvement, and these he listed as "improved." In my series, however, these are "improved" when acuities become 2/200 or better.

Any eye which loses 25 percent of its preoperative vision is "worse," and all eyes with results between three-fold improvement and 25 percent loss are "unchanged."

RESULTS IN 100 CONSECUTIVE CASES

In this series 73 percent had clear or fairly clear grafts and worth-while visual improvement one year later. When the cases

TABLE 2

VISUAL RESULTS IN 100 CONSECUTIVE CASES

	Percent
After 1-year follow-up	
Improved	73
Unchanged	15
Worse	12
After full follow-up of 1 to 10 years (Average = 6 years)	
Improved	69
Unchanged	19
Worse	12

were followed as long as possible, however (average follow-up in this series was six years), the percentage of clear grafts decreased because of late complications, including late edema, recurrence of the original pathology, or new corneal disease such as dendritic keratitis. With this long follow-up, the percentage of "improved cases" fell to 69 percent (table 2).

KERATOCONUS

When considered by groups (table 3), the highest percentage of success has been in keratoconus eyes. Conical corneas were grafted only in extreme cases where the apex was very cloudy and contact lenses were not usable (fig. 26C and D). Of only 13 done, the poorest result had 20/70 acuity. Nine eyes had 20/30 or better with ordinary glasses. This was the only clinical group with 100 percent success and this figure will undoubtedly fall markedly as other eyes are done.

Incidentally, the 20/70 eye is the one with marked ectasia and the opacity of the entire cornea described earlier in the discussion of preliminary pressure bandaging. Original vision was perception of shadows only. The fellow eye has also been grafted and has 20/20 acuity. This gentleman is now doing full time clerical work.

NODULAR DYSTROPHY AND LATTICE KERATITIS

Of 25 nodular dystrophy (fig. 26A and B) and lattice keratitis cases (24 from 100-case series, one from early series), all but five had worth-while improvement (79 percent in this series, 80 percent in combined series). These familial dystrophy cases are particularly interesting, as there were several families each with several grafts in the family.

In one lattice keratitis family I did eight grafts, seven of them very successful, the eighth with partial improvement. Two of these patients (Cases 31 and 35) had superficial keratectomies by Dr. Verhoeff with temporary improvement many years before he referred them for keratoplasty. This lattice keratitis family probably is unique in medical history and is being reported in detail in another paper.

TABLE 3

ANALYSIS OF RESULTS OF 100 CONSECUTIVE GRAFTS IN RELATION TO ETIOLOGY

Original Pathology	Total Cases	Improved	Unchanged	Worse	Improved (percent)	
Keratoconus	13	13			100	
Groenouw's dystrophy	13	9	3	1	69	Average for 24 dystrophy cases = 79%
Lattice keratitis	11	10		1	91	
Disciform or dendritic	16	11	3	2	69	
Interstitial keratitis	8	5	1	2	63	
Ulcers (pyogenic)	11	5	3	3	45	
Chemical burns	10	6	3	1	60	
Sclero-keratitis	4	3	1		75	
Trachoma	4	3	1		75	
Edema secondary to other corneal disease	4	0	3	1	0	
Lipoid dystrophy	1	1			100	
Salzmann's dystrophy	1	1			100	
Miscellaneous	4	2	1	1	50	

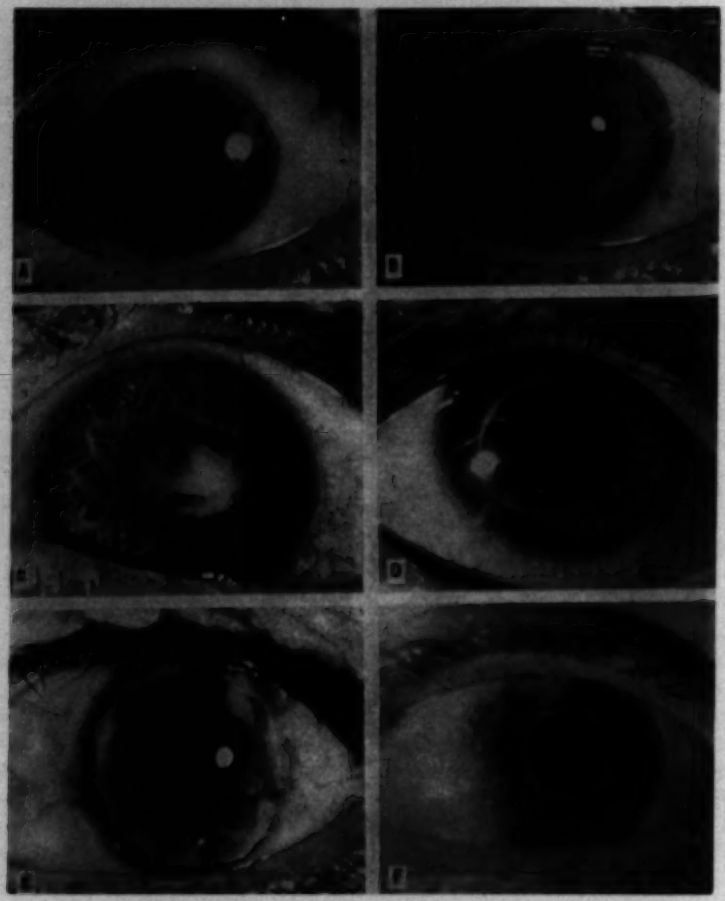


Fig. 26 A to F (Leahey). (A) Nodular dystrophy. (B) Same eye after graft. (C) Keratoconus with cloudy apex. (D) Same eye after graft. (E) Old lime burn after beta irradiation, graft, and cataract extraction. (F) Clear graft in a cornea scarred by severe phlyctenular disease 40 years earlier.

TABLE 4

ANALYSIS OF VISUAL ACUITY IN 69 IMPROVED CASES

Pathology	Number Improved	Vision 20/20 to 20/45	Vision 20/20 to 20/100	Vision 20/200 or less
Keratoconus	13	12	1	
Groenouw's dystrophy and lattice keratitis	19	12	5	2
Disciform or dendritic	11	2	3	6
Interstitial keratitis	5	1	3	1
Chemical burns	6	0	4	2
Others	15	2	10	3
Total	69	29	26	14

TABLE 5

ANALYSIS OF 12 CASES WORSE AFTER KERATOPLASTY

Pathology	Number Worse	Case Number	Preoperative Vision	Postoperative Vision
Groenouw's dystrophy	1	25	3/200	L. proj.
Lattice keratitis	1	35	2/200	Nil
Disciform or dendritic	2	42	5/200	3/200
		46	3/200	Nil
Interstitial	2	59	2/200	L. proj.
		60	6/200	3/200
Ulcers	3	78	4/200	Nil
		79	3/200	Nil
		81	1/200	L. proj.
Chemical burn	1	68	18/200	7/200
Edema secondary to corneal disease	1	86	1/200	Nil
Keratitis with iridocyclitis (Type ?)	1	98	L. proj.	L. proj.

DISCIFORM AND DENDRITIC KERATITIS

Eleven out of 16 cases of old disciform or dendritic keratitis were improved (69 percent). Since late edema in two cases and recurrence of dendritic in the graft in one resulted in some late decrease of acuity, early results were better than those reported.

CHEMICAL BURNS

Chemical burns proved more satisfactory than in some previous reports. Of 10 done, worth-while improvement was obtained in six (60 percent).

In the earlier series, however (not reported here), chemical burn cases did not

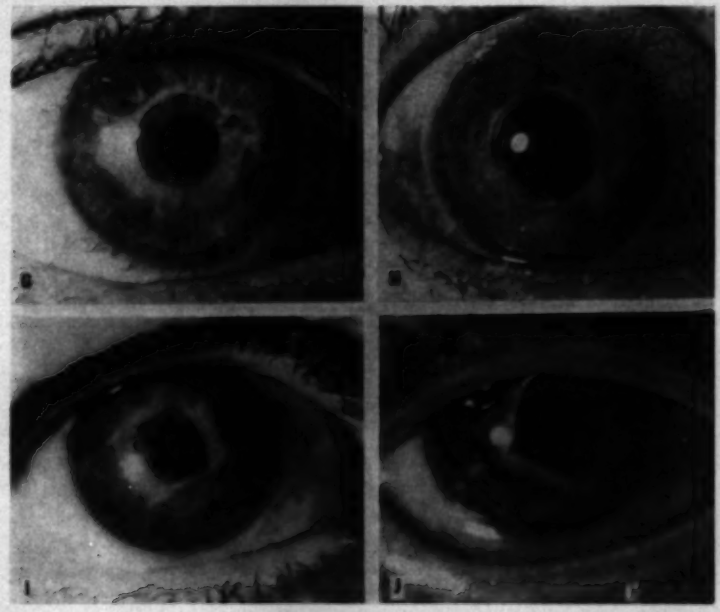


Fig 26 G to J (Leahey). (G) Graft for scars from old serpent ulcer. (H) Chemical burn after superficial keratectomy, conjunctival recession, and graft. (I) Old disciform keratitis with 4.7-mm. square graft. (J) Square graft done for keratoconus 10 years earlier.

TABLE 6

ANALYSIS OF NINE GRAFTS SUCCESSFUL AFTER ONE YEAR BUT WITH DECREASE OF ACUITY IN SUBSEQUENT YEARS

Original Pathology	Case Number	Cause of Decreasing Acuity
Lattice keratitis	28	Recurrence of lattice keratitis
Dendritic	39	Recurrence of dendritic 2 yrs. later
Serpent ulcer with Saemisch section	74	Dendritic in graft 6½ yrs. later
Chemical burn	62	Gradual edema starting 5 yrs. later
Chemical burn	68	Late edema
Edema (like Fuchs)	83	Late edema
Disciform keratitis	45	Late edema
Groenouw's dystrophy	19	Late edema
Groenouw's dystrophy	20	Late edema

have a preparatory superficial keratectomy and beta radiation. Despite some temporary success, none of these early cases could be classified as "improved."

Interstitial keratitis

The interstitial keratitis cases were a relatively unfavorable group compared to interstitial cases in general, as many of them had extreme corneal changes with some secondary lipoid dystrophy as well as other ocular pathology. Five out of eight of these were improved (63 percent).

Leucomas from pyogenic ulcers

This miscellaneous group with severe scarring included two with former perforated ulcers and one with an old serpent ulcer for which a Saemisch section had been done. Of 11 cases only five were improved (45 percent).

Edema of cornea

Four cases of marked corneal edema secondary to corneal scarring and endothelial dystrophy were included, but none of these was a true Fuchs's dystrophy. One was a complete failure; two had excellent grafts, but immediately became edematous like the host cornea. The fourth had a crystal clear graft for 13 months and then suddenly developed unexplained edema which resembled the original lesion (zero percent).

Regrafts

The results of regrafts were encouraging, as three out of nine (33 percent) were improved (table 7).

Photographs of successful primary grafts in a few other representative cases are reproduced in Figure 26E, F, G, H, I, and J.

In the 100-case series, 12 eyes were ulti-

TABLE 7

ANALYSIS OF RESULTS OF NINE REGRAFTS

Original Pathology	Case Number	Results*	Preoperative Vision	Postoperative Vision
Lattice keratitis	29	+	2/200	20/30
Disciform	44	+	L. proj.	2/200
Disciform	46	−	3/200	Nil.
Disciform	51	0	L. proj.	L. proj.
Chemical burns	69	+	7/200	20/200
Groenouw's dystrophy	20	0	7/200	20/40 for 16 mos. (7/200 later)
Groenouw's dystrophy	26	0	L. proj.	L. proj.
Edema and leucoma	85	0	1/200	2/200
Vascularized keratitis and iridocyclitis (Type ?)	98	−	L. proj.	Poor L. proj.

* + = improved; 0 = unchanged; − = worse.

TABLE 8

INCIDENCE OF POSTOPERATIVE GLAUCOMA IN 100 CONSECUTIVE CASES

Original Pathology	Number of Cases	Number with Glaucoma	Percent
Keratoconus	13	1	7
Groenouw's dystrophy and lattice keratitis	24	6	25
Disciform and dendritic	16	7	44
Interstitial keratitis	8	5	63
Old ulcers	11	5	46
Chemical burns	10	5	50
Edema, secondary to previous inflammation or disease	4	1	25
Trachoma	4	2	50
Sclero-keratitis	4	1	25
Lipoid and Salzmann's dystrophy	2	0	0
Miscellaneous	4	0	0
Total	100	33	33

mately worse than before operation. In five of these vision was reduced to nil; and in three of these unfortunate five, enucleation was actually necessary, once for infection and twice for intractable secondary glaucoma. During the past seven years, however, only one eye has been reduced to no vision, and in no case has an enucleation been needed.

SUMMARY

During the 19 years included in this 148-case series, corneal transplantation has grown from a speculative procedure to a successful and well-established ophthalmic operation. Due to continuous improvements in technique and therapy, keratoplasty is a far more successful procedure at the present time than it was even five years ago.

Among recent improvements stressed are:

1. Preoperative preparation for grafting by elimination of blood vessels by radiation, and in extreme cases by superficial keratectomy and conjunctival recession.

2. Improvements in fixation of the graft. Detailed descriptions are given of two original track suture techniques and of several new instruments, including a plastic turret style graft holder to facilitate suturing of the graft.

3. Prevention of anterior synechias, principally by the use of air in the anterior chamber, and, to a lesser extent, by improvements in graft suturing.

4. Use of steroids topically and orally for combating edema and inflammation with its attendant complications.

5. Prevention of vascularization in the new graft by reduction of inflammation and by use of beta radiation.

Technique. In most cases I use a five-mm. graft cut with a hand trephine and held in place by overlying sutures plus two direct sutures. In 5.5- to 6.5-mm. grafts overlying sutures are combined with two to four direct sutures. In grafts seven mm. or larger overlying sutures are omitted completely and the cornea is held in place by 10 to 22 direct ones.

Complications. Of the complications encountered, glaucoma was one of the more frequent, being present at some time during convalescence in 33 percent of cases.

Anterior synechias were extremely common in the early cases, but in the more recent 100-case series they occurred in only 23 percent of cases. Edema of the cornea and proliferation of connective tissue on the back of the graft were also major complications. Infection and traumatic cataract each occurred once during the entire 148-case series.

Long postoperative follow-up (19 years in some cases) suggests that progressive dystrophies of the cornea eventually recur

TABLE 9

ANALYSIS OF 100 CONSECUTIVE CASES OF PENETRATING KERATOPLASTY 1944 TO 1954

Case	Length of Follow-Up	Age, Sex, Eye	Diagnosis and Description	Preoperative Vision	Acuity after Graft	Result	Condition of Graft	Complications and Comment
1	3 yrs.	24 F R	*Keratoconus.* Marked conus with apical opacity. Has many allergies and was unable to wear any of several contact lenses.	1/200	20/30 −8.00−7.00×10	+	Clear	
2	2 yrs.	55 F L	*Keratoconus.* Mature cataract. Large apical opacities.	L. Proj.	20/35 +2.00+5.50×125	+	Clear	Had cataract extracted 5 mos. after graft with no complications.
3	6 yrs.	34 M L	*Keratoconus.* Extreme conus. Large tear in Descemets with wide opacity. Chronic irritation.	6/200 with contact 20/200	20/20 −2.25−5.00×115	+	Clear	
4	2½ yrs.	42 F L	*Keratoconus.* Vascularized scar from old cautery.	5/200 with contact 20/200, but not wearable.	20/25 −2.25−5.00×133	+	Clear	
5	11 yrs.	35 M L	*Keratoconus.* Extreme conus with marked central scarring.	1/200 20/100 with contact but not wearable.	20/25 −12.00−7.00×145	+	Clear	One year after 6-mm. square graft refractive error was −8.50 = −5.00 cyl. Myopia increased later, but no return of keratoconus.
6	5 yrs.	46 M L	*Keratoconus.* Former acute ectasia of cornea corrected by pressure bandage. Vascularized leucoma of entire cornea.	Shadows.	20/70 −3.50−2.00×60	+	Clear	Beta radiation before grafting. One anterior synechia released by miotics. Glaucoma controlled by iridectomy plus pilocarpine.
7	3½ yrs.	48 M R	*Keratoconus.* Marked conus with 3 mm. central opacity.	8/200 −4.00 cyl×165 with contact 20/50	20/20 −1.50−4.50×152	+	Clear	Other eye reported as Case 6.
8	1 yr.	22 M L	*Keratoconus.* Marked conus with 4 mm. apical opacity.	10/200 −10.00−2.00×135 with contact 20/60 (wearable only 4 hrs.)	20/25 −6.00 sph.	+	Clear	Patient has started in State Teachers College.
9	8 yrs.	20 F R	*Keratoconus.* Marked conus with 3 mm. opacity.	1/200 contact 20/60	20/30 −1.25−50×115	+	Clear	
10	2 yrs.	26 F L	*Keratoconus.* Marked conus with small central opacity.	16/200 −13.00 sph. contact 20/50	20/20 +50−2.75×45	+	Clear	Cases 9 and 10 are same patient Since the second eye was grafted, patient has passed eye test and does fine work in a large electronic plant.
11	2½ yrs.	32 R M	*Keratoconus.* Extreme vascularized leucoma of cornea due to previous cautery. Preliminary beta radiation needed.	1/200	20/40 −9.00−2.00×50	+	Clear	Myopia increased about 4 diopters during first year.
12	7 yrs.	17 M L	*Keratoconus.* Extreme conus with 4 mm. opacity.	10/200 −23.00 contact 20/70 unwearable	20/25 −5.00−2.75×45	+	Clear	
13	1 yr.	28 F R	*Keratoconus.* Moderate with only 1.5 mm. opacity. Had several prs. contacts but tolerates them only ½ hour!	3/200 −15.00 sph. contact 20/100 not wearable	20/35 −3.00−3.00×170	+	Clear	Myopia changed from +2.00 to −3.00 in first few months.
14	7½ yrs.	50 M L	*Groenouw's Nodular Dystrophy.* Numerous typical nodules with moderate gray opacity between dense spots.	5/200	20/45 −7.25−4.00×170	+	Clear	Proliferation of connective tissue on back of upper third of graft following bulging margin in that area. (Pressure dressing used, graft flattened out.)
15	6 yrs.	35 M R	*Groenouw's Dystrophy.*	12/200	20/45 −2.00−6.50×85	+	Clear	Pressure bandage used from 15th to 30th day.
16	7½ yrs.	28 M L	*Groenouw's Dystrophy.*	10/200	20/17 −4.50−3.50×98	+	Clear	Lysis of tiny anterior synechia one month later.
17	4 yrs.	23 M L	*Groenouw's Dystrophy.*	1/200	20/200 −5.00−2.50×25	+	Clear	Has incipient posterior cataract accounting for low vision (not due to graft).

TABLE 9 (*Continued*)

Case	Length of Follow-Up	Age, Sex, Eye	Diagnosis and Description	Preoperative Vision	Acuity after Graft	Result	Condition of Graft	Complications and Comment
18	7½ yrs.	42 F L	*Groenouw's Dystrophy.*	4/200	20/30 −3.00−4.00×140	+	Clear	
19	2½ yrs. (to regraft)	44 F R	*Groenouw's Dystrophy.*	3/200	7/200	0	Faint edema	Spastic entropion corrected 1 mo. later. Mild glaucoma controlled by drops.
20	2½ yrs.	47 F R	*Groenouw's dystrophy* with edema of the graft. (This is a regraft.)	7/200	20/40 For 16 mos. Late Edema 7/200	0	Variable edema	Same eye as Case 19. Preliminary iridectomy done. Perfectly clear for 16 mos., then developed edema in a single day! Vision now variable from 2/200 to 10/200. Tension normal.
21	8 yrs.	40 F R	*Groenouw's Dystrophy.* Fine white dots with irregular clouding. Cornea ⅓ normal thickness as "stripping" of cornea done 9 yrs. earlier.	2/200 −8.50−4.00×170	20/45 −12.00−4.00×170	+	Clear	Acute glaucoma on 19th day. Controlled by miotics. Lysis of small anterior synechia after one month.
22	4½ yrs.	42 F L	*Groenouw's Dystrophy.*	2/200 −8.00−4.00×145	20/100 −22.00−4.00×30	+	Clear	Donor cornea from 1½ yr. old baby. Also has incipient cataract and debris on lens surface from post-operative cyclitis.
23	5½ yrs.	45 F R	*Groenouw's Dystrophy.*	10/200	20/20+ +1.00+5.00×105	+	Clear	One quadrant of margin bulged for 3 mos., causing opacity of that area and marked astigmatism. Cylinder was 12 diopters at one time! See Figure 19.
24	8 yrs.	29 F R	*Groenouw's Dystrophy.*	4/200	20/30−2 −14.00−4.50×110	+	Clear	Sister of Case 25.
25	4 yrs. (to regraft)	33 M L	*Groenouw's Dystrophy.*	3/200	L. Proj.	−	Opaque	Graft perfect, but following lysis of anterior synechia had hemorrhage in anterior chamber and organized clot on back of graft.
26	3½ yrs.	37 M L	*Groenouw's Dystrophy* with opaque graft. (This is a regraft.)	L. Proj.	L. Proj.	0	Opaque	Has more synechia and again had bleeding at time of lysis. Glaucoma controlled by several cyclodiathermy operations.
27	1 yr.	42 M R	*Lattice Keratitis.* Diffuse lattice changes with opacities between lines. Involvement of external ⅓ of cornea.	5/200	20/20 −50−3.25×150	+	Clear	Has a few wrinkles on back of graft. Reads J-1.
28	11 yrs.	56 F R	*Lattice Keratitis.* Extreme.	1/200	20/70 −9.00−2.00×70	+	Clear	Beginning reappearance of lattice keratitis in graft 9 years later.
29	3½ yrs.	64 F L	*Lattice Keratitis.* Successful graft done 12 yrs. earlier with recent recurrence of lattice in graft.	2/200 −11.00	20/30 +5.00+2.50×165	+	Clear	Had dense immature cataract, regraft done first, and cataract extracted 5 mos. later. This is other eye of Case 28.
30	9½ yrs.	57 F R	*Lattice Keratitis, immature cataract.*	3/200	20/35 +4.50+12.00+160	+	Clear	Cataract extraction 5 mos. after graft. Beginning recurrence of lattice keratitis in graft 7 years later,
31	7 yrs.	59 F L	*Lattice Keratitis, mature cataract.* Cornea ⅓ normal thickness as corneal stripping done 8 years earlier.	L. Proj.	20/40 +8.25−2.25×35	+	Clear	Temporary elevation of graft margin controlled by pressure bandage. Acute glaucoma required posterior sclerotomy, cyclodialysis, and lysis of synechia. Cataract removed 6 mos. after grafting. No recurrence of lattice dystrophy yet.
32	6 yrs.	60 M R	*Lattice Keratitis.* Dense generalized dystrophy of cornea. Deep "wrinkles" and diffuse clouding.	4/200	20/200 −3.00−4.00×15	+	Semi-clear	Anterior synechia and acute glaucoma. Cyclodialysis and lysis of adhesions and iridectomy later. Still had chronic glaucoma, controlled by drops.
33	9 yrs.	51 M R	*Lattice Keratitis.* Had "stripping" by Dr. Verhoeff 7 years earlier with temporary improvement.	3/200	20/70 −3.00−4.00×170	+	Clear	A few permanent folds in Descemet's membrane.

TABLE 9 (*Continued*)

Case	Length of Follow-Up	Age, Sex, Eye	Diagnosis and Description	Preoperative Vision	Acuity after Graft	Result	Condition of Graft	Complications and Comment
34	4 yrs.	56 M L	*Lattice Keratitis.*	18/200	20/70 −1.00−.75×160	+	Clear	This and the previous 6 lattice keratitis eyes are all in same family. The 8th graft was done on Case 29 15½ yrs. ago and was clear for many years.
35	8 yrs.	44 M R	*Lattice Keratitis.* Superficial keratectomy done 7 years earlier.	2/200	Nil	−	Opaque	Square graft perfect at 1 month with tiny anterior synechia at three corners. Refused to have lysis! Not seen for 2 yrs., at which time eye was blind from glaucoma. Should have been a successful graft!
36	5 yrs.	63 F L	*Lattice Keratitis.*	5/200	20/70 −12.00−2.00×180	+	Clear	Extreme anterior synechia. Lysis 3 mos. later. One tiny synechia left, but has never caused trouble.
37	5 yrs.	41 F R	*Lattice Keratitis.*	7/200	20/25 −11.00−2.00×80	+	Clear	Case 37 is niece of Case 36.
38	3½ yrs.	45 F L	*Recurrent Dendritic.* Immature cataract. Dense irregular glaucoma.	4/200	5/200 −8.00−4.00×80	+ See comment	Clear	Graft crystal clear and poor vision is due to cataract. Classed as successful graft. Had glaucoma controlled by drops.
39	2 yrs.	32 M L	*Dendritic.* Dense leucoma with many vessels. Beta radiation used before operation.	18/200	20/25 −4.00−2.00×50 See comment	+	Clear	Temporary glaucoma controlled by drops. At the end of 2 years patient had new attack of dendritic in recipient cornea which soon involved graft. Present vision 9/200 but improving.
40	7 yrs.	42 F R	*Dendritic.* Dense irregular scar. Post. synechia and cyclitic membrane on lens. Incipient cataract.	2/200	20/70 +9.00+3.50×105	+	Clear	Had preliminary iridectomy. Cataract removed 6 yrs. later.
41	2 yrs.	53 M L	*Disciform.* Dense disciform opacity 8 mm. wide with a few vessels.	2/200	20/70 +5.00−10.00×45	+	Clear (except in lower third)	Had glaucoma before grafting controlled by cyclodiathermy. Glaucoma again after grafting controlled by one cyclodiathermy and drops. Bulging lower graft margin accounted for astigmatic error.
42	10 yrs.	47 F L	*Disciform.* Dense wide leucoma with a few superficial and deep vessels.	5/200	3/200 +9.50+2.00×150	−	Semi-clear	Traumatic cataract noticed during convalescence (from keratome incision in square graft?) Most of cataract absorbed but further surgery never done.
43	2 yrs. (to regraft) (see 46)	46 F R	*Disciform.* Bullous keratitis, chronic glaucoma. Cataract, complete posterior synechia. Former chronic uveitis.	L. Proj.	L. Proj.	0	Marked edema	Iridectomy and two cyclodialyses for glaucoma and adhesions done first. Glaucoma recurred after graft. One cyclodialysis and two cyclodiathermies done with control of tension.
44	1½ yrs.	48 F R	*Disciform.* Edema of cornea and graft. This is regraft of Case 43.	L. Proj.	2/200 +10.00	+	Faint edema of epithelium	Graft clear for for 6 mos. and tension normal. Cataract removed. Faint edema of graft since then. One new cyclodiathermy was needed.
45	2½ yrs. (to regraft) (see 48)	56 F L	*Disciform.* Very thick scar 10 mm. wide with a few deep vessels.	L. Proj.	20/25 +3.00−7.00×160 1 yr. later 3/200 2 yrs. later	+	Clear for 1 year. Edema later	Graft crystal clear for 12 months then within 2-day period showed marked edema.
46	9 yrs.	58 F L	*Disciform.* Edema of old graft. This is regraft of Case 45.	3/200	Nil	−	Opaque	Violent nausea first day postop. Nonunion of lower margin of square graft. Conjunctival flap later. Extensive anterior synechia and glaucoma.
47	8½ yrs.	23 M L	*Dendritic.* Irregular central scar 8 mm. in diameter.	7/200	20/200	+	Clear centrally	Proliferation of connective tissue on posterior graft surface except for 2 mm. centrally. Much aberration.
48	2½ yrs.	52 F F R	*Recurrent Herpes* (?). One ulcer cauterized 5 yrs. earlier. About 30 irreg. punctate scars and 2 larger ones. Extreme aberration.	1/200	20/25 −9.00−2.00×180	+	Clear	Other eye also has corneal scarring, but patient has been able to resume school teaching (which she had given up years ago).
49	4 yrs.	60 F L	*Disciform* with secondary fatty dystrophy and calcification. Immature cataract.	L. Proj.	8/200	+	Clear	

TABLE 9 (*Continued*)

Case	Length of Follow-Up	Age, Sex, Eye	Diagnosis and Description	Preoperative Vision	Acuity after Graft	Result	Condition of Graft	Complications and Comment
50	2 yrs. (to regraft) (see Case 51)	60 F R	*Disciform.* Large dense full thickness corneal leucoma. Immature cataract.	L. Proj.	L. Proj.	0	Edema	Marked psychosis. Up and about first night, bandages pulled off! Discharged without eye pad on third day! Extensive anterior synechia but graft healed firmly. Lysis of synechia done later.
51	3½ yrs.	62 F R	*Disciform.* Edema of old graft. Immature cataract. (This is regraft of Case 50.)	L. Proj.	L. Proj.	0	Edema	Because of previous psychosis, direct sutures used, and patient uncovered in two days. Graft perfect with no synechia, but faint edema present early became marked in 6 months.
52	8 yrs.	64 M L	*Disciform.* Dense leucoma 7 mm. wide centered temporally. Immature cataract.	L. Proj.	6/200 −7.50 sph.	+	Clear	Has myopic retinitis. Poor vision principally from cataract, however. Counted as "improved" as graft is perfect and tension is normal.
53	6 yrs.	63 M R	*Disciform.* Deep opacities 8 mm. wide. Many vessels before use of beta.	2/200	20/50 −2.50 −6.00 X 10	+	Clear	Old debris on lens surface reduces vision.
54	6½ yrs.	63 F R	*Interstitial Keratitis.* Diffuse opacity of entire cornea. Faint vessels.	8/200	20/60 −6.00 cyl. X 130	+	90% Clear	Recurrence of typical interstitial keratitis in host and graft with eventual almost complete clearing of graft. Glaucoma later, controlled by drops.
55	4 yrs.	15 F R	*Interstitial keratitis.* Diffuse irregular scarring. Many old "ghost" vessels. Old debris on lens surface.	1/200	20/70 −14.00 −2.00 X 166	+	Clear	Recurrence of interstitial in graft —controlled by systemic cortisone. Chronic glaucoma controlled by pilocarpine and Floropryl.
56	1 yr.	18 F L	*Interstitial Keratitis.* (Other eye of Case 55.) Extensive dense opacity with tiny old vessels—a few still patent.	1/200	20/40 −4.50 cyl. X 75	+	Clear	Was given systemic cortisone starting on 5th day. No recurrence of interstitial.
57	7 yrs.	30 F R	*Interstitial Keratitis.* Wide dense gray scar with some secondary lipoid dystrophy.	2/200	20/70 −2.00 X 80	+	80% Clear	Done before cortisone was available. No unusual inflammation. Poor vision due to old cyclitic debris on lens surface and slight lens opacities.
58	11 yrs.	32 F R	*Interstitial Keratitis.* Almost total opacity of cornea. Previous chronic glaucoma of each eye.	2/200	15/200	+	Clear in 1 mm. area only	Proliferation of connective tissue over back of entire graft except for area 1 mm. square. Glaucoma controlled by drops. Can read newsprint with +4.00 lens!
59	11 yrs.	63 M R	*Interstitial Keratitis.* Also probable disciform keratitis. Dense 7 mm. leucoma centrally. Faint scarring in periphery.	2/200	L. Proj.	−	Opaque	Very uncooperative during and after operation. Extensive anterior synechia and a 1 mm. iris prolapse. Conjunctival flap. Cyclodialysis later. Glaucoma controlled by drops.
60		M R	*Interstitial Keratitis* with extensive anterior synechia! Dense scarring of most of cornea.	6/200	3/200	−	Semi-Clear	Had lysis of anterior synechia before graft. Glaucoma later controlled by one cyclodiathermy and drops.
61	10 yrs.	35 M R	*Interstitial Keratitis.* Bluish white opacity of entire cornea. Some fatty degeneration. Pupil not visible.	L. Proj.	L. Proj.	0	Opaque	Graft healed well. Obstinate glaucoma. Cyclodialysis and trephine operation done. Glaucoma now moderately well controlled with drops.
62	11 yrs.	55 M L	*Chemical Burn* (Lime) 40 yrs. earlier. Complete leucoma. A few vessels.	L. Proj.	20/70 +5.00 sph. for 4 years. 3/200 after 11 yrs.	+	Clear for 4 years. Faint edema since then	Dense yellow leucoma with fatty degeneration. Graft very clear 4 yrs., then faint edema in stroma and epithelium. Gradually worse. Mild glaucoma controlled by drops.
63	5 yrs.	61 M R	*Lime Burn.* (46 yrs. ago). Dense thick heavily vascularized pannus of entire cornea. Had superficial keratectomy, resection of limbal scar tissue and beta.	L. Proj.	20/60 +4.00 −6.00 X 180	+	Clear	Glaucoma controlled by drops. This is other eye of Case 62. Is beginning to show stromal changes suggesting eventual trouble as in left eye.

TABLE 9 (*Continued*)

Case	Length of Follow-Up	Age, Sex, Eye	Diagnosis and Description	Preoperative Vision	Acuity after Graft	Result	Condition of Graft	Complications and Comment
64	3 yrs.	24 M L	*Lime Burn*. Complete pannus and dense leucoma of entire cornea.	L. Proj.	20/60+ +1.50+4.00×145	+	70% Clear	Superficial keratectomy, recession of scar tissue and conjunctiva from limbus, and beta radiation before grafting.
65	2½ yrs.	25 M L	*Ammonia Burn* (from explosion). Complete dense white heavily vascularized leucoma.	L. Proj.	2/200	+	25% Clear	Superficial keratectomy and beta first. Patient's body jerks constantly, so operation done under general. Graft vascularised and was given beta later. Glaucoma controlled by drops.
66	2 yrs.	40 M R	*Chemical Burn* (Caustic Soda). Dense white leucoma of entire cornea with many vessels.	L. Proj.	1/200	0	Central 2 mm. translucent	Superficial keratectomy and beta first. Bulging of graft and poor union inferiorly required pressure bandage, with eventual well healed margin.
67	2½ yrs.	27 M R	*Lime Burn*. Deep vascularized leucoma of 50% of cornea and superficial scarring of remainder.	3/200	20/60 −8.00−4.00×180	+	Clear	Superficial keratectomy followed by beta radiation.
68	3½ yrs. (to regraft)	32 M R	*Ammonia Burn*. Irregular scarring of most of cornea with many deep and superficial vessels.	18/200	20/70 −7.00−4.00×180 1 yr. later 7/200 3 yrs. later	−	Clear for 15 mos. Faint edema later	Much beta before grafting. Also cautery to larger vessels at limbus. After late edema appeared to be permanent, regraft advised.
69	1½ yrs.	36 M R	*Ammonia Burn* with edema of graft. This is regraft of Case 68.	7/200	20/200 −3.00−3.00×150	+	70% Clear	Considerable proliferation of connective tissue on back of graft with irregular astigmatism.
70	6½ yrs.	48 M L	1918 explosion and *Chemical Burn*, type unknown. Complete vascularized leucoma.	Shadows See comment.	5/200 −6.00−4.00×165	0 See comment	Semi-Clear (Faint edema)	Iridectomy and beta before grafting. Glaucoma controlled by drops after grafting. Vision improved to 4/200 after iridectomy and beta before graft, so graft result classed as o.
71	11 yrs.	55 M L	*Lime Burn*. Diffuse deep opacities and degenerative changes. A few old vessels.	L. Proj.	1/200	0	Slightly Cloudy	Diathermy peritomies to occlude vessels before operation and preliminary iridectomy. Glaucoma controlled by drops.
72	11 yrs.	15 M L	*Corneal Ulcers* in infancy. Diffuse irregular scarring. A few small vessels. Nystagmus. Amblyopia.	Shadows	Shadows	0	Cloudy	Had peritomy with diathermy beforehand to reduce vascularization. One posterior synechia at corner of square graft.
73	7 yrs.	60 F L	*Ulcers* in childhood. Dense irregular scarring. No vessels. High myopia. Incip. cataract.	2/200	"Can see well." Data not available.	+	Clear	Tiny incarcerated iris prolapse. Excision with conjunctival flap 6 wks. later. Lysis of synechia twice. Cataract extraction 8 mos. after graft. Follow-up by letter from California, "can see well." No data given.
74	7 yrs.	51 M L	*Serpent Ulcer* with hypopyon. Saemisch section done. Dense vascularized leucoma.	1/200	20/35 +12.50+2.50×40	+	Clear for 6½ yrs. Cloudy now due to recent dendritic.	Peritomies and beta first to remove vessels. Cataract extraction later. Clear graft for 6½ yrs. Dendritic keratitis in 1955 affected host cornea and graft. Present vision 4/200 but improving. Permanent scarring of graft!
75	8 yrs.	36 M L	*Ulcer* in infancy. Dense leucoma over nearly entire cornea. Nystagmus. Amblyopia.	3/200	15/200	+	Faint edema	Temporary glaucoma controlled by drops.
76	9 yrs.	39 F L	Perforated *Corneal Ulcer*. Dense leucoma of most of cornea with anterior synechia. 3 small vessels.	L. Proj.	L. Proj.	0	Very Opaque	Diathermy peritomy first. Almost complete anterior synechia after graft. Lysis done twice, and 1 iridectomy. Chronic glaucoma not well controlled.
77		56 F R	Recurrent *Corneal Ulcer* since childhood. Dense irregular scarring. Immat. cat. High myopia	3/200 −11.00	5/200 +8.00	0	70% Clear	Glaucoma controlled by pilocarpine. Cataract extraction 1 yr. later. Ectasia of cataract scar with repair 6 mos. later.

TABLE 9 (*Continued*)

Case	Length of Follow-Up	Age, Sex, Eye	Diagnosis and Description	Preoperative Vision	Acuity after Graft	Result	Condition of Graft	Complications and Comment
78	9 yrs.(?)	30? M ?	*Corneal Ulcer* in childhood. Dense irregular scarring.	4/200	Nil	−	Enucleation	Severe iridocyclitis, pain, and secondary glaucoma. Cortisone or cyclodiathermy not available at that period. Enucleation several weeks later. Details from memory as record not available.
79	8½ yrs.	50 M L	*Recurrent Ulcers.* Dense irregular scar 7 mm. wide. A few tiny vessels.	3/200	Nil	−	Enucleation	Panophthalmitis on 3rd day. Donor eye from a distant small hospital, and not removed by ophthalmologist. Infection probably introduced with graft. This is only infection in 148 cases. Since then all donor eyes washed in three basins of saline at time of operation.
80	6 yrs. (till death 2 yrs. ago)	61 F L	*Recurrent Ulcers* in childhood. Diffuse dense scarring. No vessels. Immature cataract.	1/200	20/60 +7.00+6.00×125	+	Clear	Cataract extraction done 5 mos. later.
81	5½ yrs.	56 M R	*Recurrent Corneal Ulcers.* Dense scarring of most of cornea. Many vessels. Immature cataract.	1/200	L. Proj.	−	Cloudy	Vessels removed by beta radiation before operation. Lower border of graft elevated with nonunion. Healed well with pressure bandage. Extensive anterior synechia inferiorly. Tension normal. Lysis and regraft advised but patient has not consented.
82	5 yrs.	75 M R	*Recurrent Ulcers* with secondary lipoid dystrophy. Mature cataract.	L. Proj.	L. Proj.	+ See comment	Clear	Intestinal obstruction after graft with abdominal operation on 10th day. Mature cataract found. Discharged to convalescent home with clear graft. In 1951 (5 yrs. later) patient still alive, with clear graft, but cataract never removed.
83	8 yrs.	39 F R	*Edema of Cornea*—severe—secondary to blow from stone 12 yrs. before. Tear in Descemets across entire cornea. Eye constantly irritated.	1/200	20/60 +5.00+4.50×170 (for 13 mos.) 3/200 (after 8 yrs.)	0 See comment	Clear 13 mos. Marked edema now	Crystal clear for 2 years; then sudden edema coming on in 2 days! Graft now resembles remainder of cornea but slightly less edematous.
84	6 yrs. (to regraft)	F L	*Faint Edema of Cornea.* Large dense leucoma. Anterior and post. synechia. Old iridocyclitis. Immature cataract.	2/200	1/200	0	Faint edema	Lysis of synechia before grafting. Glaucoma after grafting controlled by drops. Graft perfect, but showed faint persistent edema.
85	2½ yrs.	F L	*Edema of Cornea and graft.* This is regraft of Case 84.	1/200	2/200	0	Very faint edema	Excellent graft, but again shows persistent very faint edema, so cataract extraction not attempted.
86	8½ yrs.	76 F R	*Marked Edema and Dystrophy of Entire Cornea,* resembling Fuchs' dystrophy. Old scar. Immature cataract.	1/200	Nil	−	Edema	Spastic entropion immediately after graft. Flat chamber. Anterior synechia. Glaucoma. Patient did not return for follow-up surgery. Enucleation elsewhere 3 yrs. later because of painful glaucoma.
87	5 yrs.	51 M R	*Old Trachoma.* Diffuse scarring of entire cornea with dense leucoma over pupil. Many small vessels.	20/200 −7.00 sph.	20/200 −6.00−5.00×90	0	80% Clear	Beta radiation before and after operation. Severe postoperative inflammation. Pressure bandage for bulging graft. Clear graft, but irregular areas of connective tissue proliferation on posterior surface cause aberration.
88	4 yrs.	50 F R	*Old Trachoma.* Irregular diffuse scarring with numerous superficial vessels.	5/200	20/150 −4.00−2.00×45	+	Clear	Beta radiation first. Graft clear but vision reduced by postcortical cataract. Postoperative glaucoma controlled by pilocarpine and one cyclodiathermy.
89	4½ yrs.	49 F R	*Old Trachoma.* Irregular dense scarring. A few vessels. Slight microphthalmos. Incipient cataract. Hypertension (220/140).	L. Prof.	20/100 0 correction (Reads V-2)	+	Clear	Glaucoma controlled by one iridectomy, one cyclodiathermy, and drops.

TABLE 9 (*Continued*)

Case	Length of Follow-Up	Age, Sex, Eye	Diagnosis and Description	Preoperative Vision	Acuity after Graft	Result	Condition of Graft	Complications and Comment
90	7 yrs.	60 M R	*Old Trachoma.* Dense opacity of entire cornea. Some secondary lipoid dystrophy. A few vessels. Immature cataract.	Shadows	20/60 +6.25+4.00×18	+	Clear	Cataract extraction 6 mos. later. Media clear but has old chorioretinitis scar involving part of macula area. Other eye has no vision, but patient now working as barber!
91	10½ yrs.	55 F R	*Sclerokeratitis* with secondary fatty dystrophy. Dense white scarring. No vessels. Chorioretinitis (found later).	Shadows	4/200	0	70% Clear	Uneventful convalescence. Irregular astigmatism in graft. Large patch of chorioretinal degeneration prevents better acuity. Graft clear enough to give 20/200 vision.
92	8½ yrs.	50 M L	*Sclerokeratitis.* Also recurrent ulcers(phlyctenular keratitis?) in childhood. Diffuse irregular dense scars, no vessels.	4/200	20/100 −5.00 cyl. ×15	+	Clear	Fundus seen clearly so poor vision due to amblyopia exanopsia. Had tiny area of dendritic keratitis on graft 8 yrs. later with no permanent visual effect.
93	1½ yrs.	39 F R	*Sclerokeratitis.* Many recurrent attacks (as was true of other cases also). Former Tbc. iridocyclitis. Diffuse deep scarring with moderate deep vascularization.	2/200	20/200 −3.00−1.50×90	+	70% Clear	Had densitization with old Tbc. several years before. Beta radiation to remove vessels. No marked inflammation after graft. Several tiny deep infiltrates in graft prevent better vision.
94	4 yrs.	34 F L	*Sclerokeratitis.* Dense white scar covering upper 70% of cornea. A few deep vessels.	3/200	20/70 −9.00−2.00×75	+	Clear	Graft crystal clear, but eye has had intermittent glaucoma attacks. Gonioscopy shows extensive peripheral anterior synechia. Tension controlled by four cyclodiathermies plus drops.
95	10½ yrs.	57 F L	*Lipoid Dystrophy.* Full thickness yellow-white fatty degeneration of 70% of cornea including pupillary area.	5/200 10/200 (dilated)	20/40 +1.25−1.50×100	+	Clear	Anterior synechia at 2 corners of square graft freed by lysis later. Graft clear with slight lipoid changes in one corner only after several years. Lipoid dystrophy in remainder of cornea has improved since grafting!
96	3 yrs.	46 F L	*Salzmann's Dystrophy.* Childhood phlyctenular keratitis. Ridge like lesions, vascularized slightly. Diffuse opacities of rest of cornea.	7/200 −12.00	20/70 −17−4.00×150	+	Clear	Crystal clear graft. Poor vision due to myopic type fundus degeneration with involvement of paramacula area.
97	2 yrs. (to regraft)	64 F L	*Recurrent Keratitis* and *Iridocyclitis*, type unknown. Dense extremely vascularized leucoma. Mature cataract. Complete posterior synechia.	L. Prof.	L. Proj.	0	Opaque	Superficial keratectomy and beta radiation before grafting. Graft excellent, but chamber lost when sutures removed, and anterior synechia formed. Graft vascularized later.
98	1½ yrs.	66 F L	*Vascularized Leukoma* and opaque corneal graft. Mat. cat. Anterior and posterior synechia. Regraft of case 97.	L. Proj.	L. Proj. (Slightly defective)	−	Opaque Vascularized	Had more beta after first graft in preparation for this. Graft technically perfect, but recurrence of iridocyclitis for 2 mos. Eye now white but tension is abnormally low.
99	1[illegible] yrs.	26 M R	*Metaplasia of epithelium of Cornea and Conjunctiva.* Complete vascularized opacity of entire cornea with dry scaly appearance as in pemphigus. Extreme vascularization, deep and superficial.	L. Proj.	20/60 0 correction	+	Clear	Superficial keratectomy, recession of scar tissue from limbus and beta radiation. Diagnosed in Greece as "Malignant vernal catarrh," but diagnosis not confirmed here. Patient kept on topical hydro-cortisone and vitamins. No evidence of recurrence.
100	1½ yrs.	26 M L	*Metaplasia of Epithelium of Cornea and Conjunctiva.* Other eye of Case 99. Similar picture but much less extreme.	1/200	20/80 0 correction	+	Clear	Superficial keratectomy, recession of scar tissue for 4 mm. from limbus, and beta radiation. One anterior synechia, with lysis one month later. Some connective tissue proliferation on back of graft.

in the new cornea at the same rate as in the original cornea. Since time required for reappearance is usually many years, the probability of recurrence is not a contraindication to grafting.

Results. Results of the entire 19-year series of 148 cases were 63.5 percent "improved." Recent results are much better than those of the 1930s; and, for the sake of current statistics, analysis is presented of 100 consecutive grafts (91 primary and nine regrafts) done in recent years. In this series, running from 1944 to 1954, results were 69 percent "improved," 19 percent "unchanged," and 12 percent "worse."

In this latter series, results in "most favorable cases" (keratoconus, nodular dystrophy, and lattice keratitis) were excellent, with 32 out of 37 being improved (86.5 percent). By etiologic groups, results were as follows: keratoconus, 100 percent; nodular dystrophy and lattice keratitis, 79 percent; interstitial keratitis, 63 percent; disciform and dendritic keratitis, 69 percent; leucomas from pyogenic ulcers, 45 percent; chemical burns, 60 percent; edema of cornea (similar to but not true Fuchs's dystrophy), zero percent; regrafts (miscellaneous), 33 percent.

Since the results in this 100-case series are better than those of the previous seven years, and since the results during the past few years have been better than those in the first part of the series, it is reasonable to expect that transplant statistics will continue to grow more favorable for many years to come.

9 Central Street.

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Ophthalmic Miniature

The principle of increased pressure, from which standpoint v. Graefe interpreted all the symptoms of glaucoma, still holds good, although we now know that increased pressure in itself is not the primary cause of glaucoma, but is the result of some fundamental disease depending on circulatory disturbance.

A. Mooren, *Arch. Ophth.*, 13:15, 1884.

SURGERY FOR SENILE MACULAR DEGENERATION*

RONALD M. BURNSIDE, M.D.
Dallas, Texas

The incidence of senile macular degeneration for a two-year study, with over 2,000 patients surveyed, indicates that senile macular degeneration is probably the third most common cause of blindness. Table 1 gives the complete study:

TABLE 1

SENILE MACULAS
PATIENTS OVER 40 YEARS OF AGE
July 1955–June 1957
2,075 Patients

Ratio	Total	Type of Disease
1:7	292	Early—20/30 less
1:25	80	Advanced—20.30 greater
1:25	84	Advanced—with cataract
1:12	164	Advanced
1:6	356	Senile maculas

Evaluation of the surgery in the treatment of senile macular degeneration, on the basis of increased blood supply to the choroid from the inferior oblique muscle, has been studied by tracer methods through the use of phosphorous isotope 32. A nine-month study using dogs with a macular disturbance produced in one eye by macular burn from direct sunlight and followed by inferior oblique surgery on the same eye with the opposite eye used as a control has been completed.

Technical problems of Geiger counts with the present probes were, on the whole, unsatisfactory for study of the posterior segment of the eye. A large counter probe, modified with a slender column of plastic window placed between the recti muscles and back of the ciliary body directly over the conjunctiva, was not fully reliable for repeated counts.

It was found that the volume of choroid blood flow diminishes in the first 30-day period after macular burn, to return to normal at 60 days, and to remain at normal for six months, the time of the final flow counts. No repeated counts were above normal, and possibly should not be expected. Counts directly over the anastomosis did not diminish at the end of six months, suggesting that the vessels are not replaced by fibrosis over this period of time. P^{32} counts on a patient three months postoperative likewise were not entirely satisfactory, but did indicate a normal choroidal flow, but not above the rate in the opposite eye.

We must await better and smaller Geiger counters or the use of very sensitive dosimeters to obtain more reliable readings. These minute dosimeters may be placed behind the macula or on the edges of a lacrimal contact lens for more consistent readings in the posterior segment of the eye.

The surgery is usually done under local anesthesia, using a four-percent Novocaine retrobulbar injection with additional local infiltration along the lateral rectus muscle. The operative procedure is as follows:

The lateral rectus is divided and 4-0 silk is placed on the upper and lower edges of the tendon-stump to aid the patient to look medially and slightly superiorly. The lateral rectus tendon is marked with the usual sutures for its replacement, and laid aside. Tenon's capsule is opened from the lateral margins of the superior and inferior recti in the usual manner. Occasionally, a horizontal incision may be extended along the inferior border of the lateral rectus. A lateral canthotomy is required at times to increase the exposure. Perhaps the section of the check ligaments of the medial rectus may be indicated occasionally, but has not been necessary to date. It has been found

* Presented before the sectional meeting of the American College of Surgeons, Dallas, Texas, January 10, 1958. This paper is a continuation of a previous study, Am. J. Ophth., **42**:6 (Dec.) 1956.

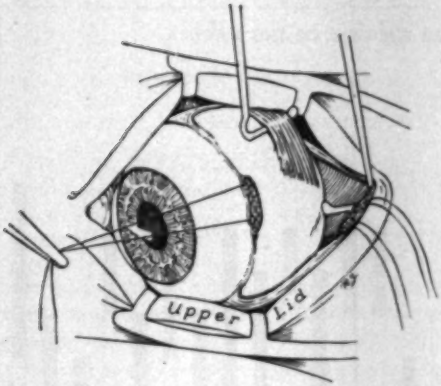

Fig. 1 (Burnside). The lateral rectus has been sectioned, with traction sutures placed on its tendon. Tenon's capsule opened, with a squint hook on the inferior oblique.

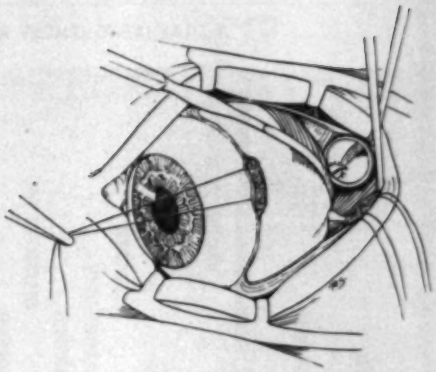

Fig. 2 (Burnside). Size 2-0 mirror in place to visualize iris repositor touching optic nerve and measuring the distance to the inferior oblique muscle.

that a squint hook offers the best exposure to visualize the retrobulbar space with the aid of a 2-0 laryngeal mirror. If the operator moves his head, the optic nerve, ciliary vessels, and especially the long ciliary artery may be seen in the mirror.

Placing the squint hook tip against the sclera over the path of the long ciliary artery makes it more prominent and injury less likely. A co-operative patient can describe metamorphosis of objects in the operating room when the sclera, over the macula, is touched by the squint hook. An iris repositor, curved to the shape of the eye with grooves on the edges at mm. intervals, should be placed against the optic nerve with one edge over the medial border of the inferior oblique muscle at its insertion.

The direct line of scleral suture should then be determined at the three to four-mm. mark on the repositor. A concave mirror instead of plano mirror, if available, would extend the field of vision of the operator, and he would not have to move his position. Touching the optic nerve divides the adventitious sheath, a reflection of Tenon's capsule around the short ciliary vessels which, if left intact, may prevent the ingrowth of new vessels.

A figure-eight locked 6-0 chromic suture is placed in the medial border of the inferior oblique muscle and the medial half of the muscle is cut from the sclera. The line of insertion of the oblique muscle is most frequently widened, rather than advanced; thus, diplopia should not be expected. The scleral suture is placed at the predetermined site and tied. The lateral rectus is replaced, and the conjunctiva with tendons is closed in the usual manner.

Figures 1, 2, and 3 illustrate the present

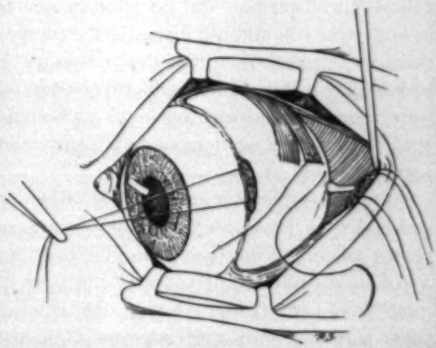

Fig. 3 (Burnside). Suture of 6-0 chromic placed in medial part of inferior oblique muscle and medial one half cut from insertion. Posterior arm suture placed in sclera over macula.

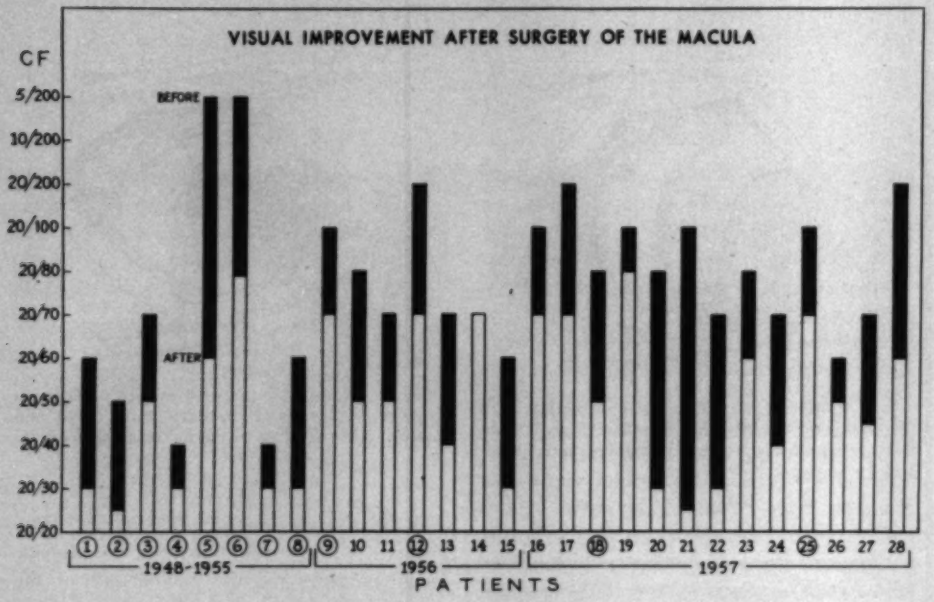

Fig. 4 (Burnside). Results.

surgical technique, which can be modified from time to time for the sake of better visualization and operative safety in this critical area of the eye.

The block graph shows the present series of patients operated to date. Naturally, the 1957 patients have not had enough time to evaluate the final results, but they will be followed to determine the variation of vision in both eyes. Should the vision in the unoperated eye become less than the vision in the operated eye the result could be considered significant. Should any come to pathologic studies for serial sections, a final conclusion may be drawn.

Apparently there is no short cut objective procedure to determine the value of surgery on the macula to increase choroidal flow, but a follow-up of several years is the present method of evaluation. During the coming year patients with arteriosclerosis in the retinal vessels will be offered combined posterior sclerotomy beneath the advanced muscle to increase further the anastomosis of vessels to the choroid.

In the future correction of the faulty metabolism may offer the solution of this problem and surgery for the arteriosclerotic disease may no longer be necessary. The anastomosis of the inferior orbital to the ophthalmic artery may be of value if this more simple supply of vessels does not prove satisfactory. It may be worthwhile to tie off the infraorbital artery as it emerges from the infraorbital canal to increase the blood flow to the inferior oblique muscle, and thus to the anastomosis site, with further collateral blood flow from the external carotid artery.

4105 Live Oak (21).

I wish to thank Jack K. Jeanes, Ph.D., Department of Biophysics, Southwestern Medical School, Dallas, Texas.

NOTES, CASES, INSTRUMENTS

DeWECKER SCISSORS

In removing corneal-scleral sutures

Albert C. Esposito, M.D.
Huntington, West Virginia

To find an instrument which could be more easily manipulated during removal of corneal scleral sutures has been my goal for quite some time. In 1946, I stumbled upon the use of a standard pair of DeWecker scissors for this purpose. Since that time, I have found that the DeWecker scissors are ideally suited for the job.

The surgeon is at the head of the patient. With the eye open and the patient looking downward, after local pontocaine anesthesia has been administered, the DeWecker scissors are used. The upper lid is retracted with the index finger of one hand while the DeWecker scissors are held in the other. The sharp-pronged blade is inserted in the loop of the suture and the blades are closed quickly, cutting the corneal-scleral sutures speedily and easily. This is facilitated by the blades being at right angles to the shaft; they seem perfectly adapted for this procedure.

Although the DeWecker scissors were originally planned for the iridectomy, they can be used for the modern types of corneal-scleral sutures, eliminating the need to use catgut suture if the surgeon so desires. The method is simple and easily performed. Because the blades of the scissors are angled, their manipulation is simple, as I have found in my practice.

1212 First Huntington National Bank Building (1).

Fig. 1 (Esposito). DeWecker scissors in position, ready to cut the corneal-scleral sutures. Note the right angulation of the blades which seem to make them perfectly adapted for this procedure.

Fig. 2 (Esposito). DeWecker scissors in position, showing the ease with which the sutures can be cut with the right-angled DeWecker scissor blade.

WHITE SPOTS OF THE IRIS

M. F. Mueller, M.D.
New York

White spots on the iris may be present in different conditions: (1) the pigment of the stroma may disappear in spots in cases of glaucoma; (2) the same may happen if pieces of lens matter remain for some time on the surface of the iris;[1] (3) many white spots may remain if the patient has had smallpox (vitiligo iridis, L. Mueller[2]); (4) after recovery from a chronic tuberculous iritis some white spots may remain (Michel's spots[3]). However, all these spots show a slight concavity.

In normal irises one may encounter tiny white spots in the outmost periphery. I en-

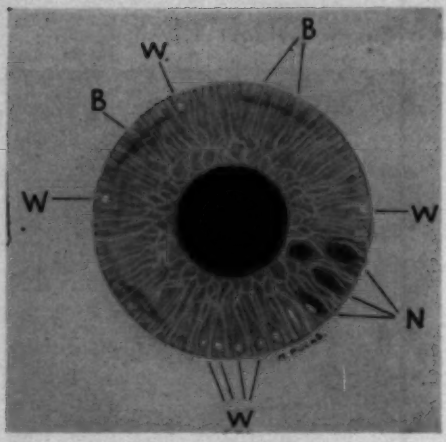

Fig. 1 (Mueller). Brushfield spots of the iris, right eye. (W) Warts (N) Nevi. (B) Pigment bands.

countered such a case some years ago and was able to get a picture of it, which I owe to Mrs. Fuchs. As this type of white spots is not too frequent I want to report it:

Case report

A white woman, aged 68 years, came to see me because of poor vision. Her vision was 20/100, right; 20/100, left. The cornea showed a severe endothelial dystrophy which looked brownish and showed a streaky pattern. The affected endothelium was in the center of the cornea, leaving the limbal region more or less free.

The iris of the right eye was blue and its periphery had nine round whitish tiny dots, which on slitlamp examination appeared elevated (fig. 1). In the lower periphery they were situated in regular intervals, in the rest of the iris at the 3-, 10-, and 11-o'clock positions. Besides these whitish spots there were, on the temporal side, at the 10- and 7-o'clock positions, brownish indistinct bands which were much broader than the white dots and corresponded to the site where, as a rule, the ciliary crypts are found. Four brownish nevi of medium size, more or less in the area of the minor circle of the iris, were also found.

The iris of the left eye showed almost the same pattern. Here the white spots were at the 3-5- and 8-o'clock positions. There were two brownish nevi in the periphery at the 4- and 7-o'clock positions and two smaller ones near the periphery at the 8- and 9-o'clock positions. There were faint bandlike pigmentations at the 3- and 9-o'clock positions.

Because these white spots startled me, I scanned the literature for reports. Vogt in his *Spaltlampen-Mikroskopie* does not mention them. Berliner in his *Biomicroscopy of the Eye*[4] gives a picture in which peripheral small yellow spots are present on the iris, apparently lying deep in the stroma. He describes these spots and calls them Krückmann-Wölfflin bodies and adds "in cases of iridocyclitis they have been incorrectly interpreted as inflammatory nodules. Comparison with the unaffected eye will serve to correct such an error." Krückmann describes them as "knoblike condensations, brown, yellowish, or whitish. In dark brown irises they appear darker, in irises lighter in color, yellow or white. They are best seen in direct light, usually in both eyes."

The white peripheral spots of the iris are of special interest, as in 1924 Brushfield,[5] an English pediatrician, discovered signs which in their plurality made the early diagnosis of mongolism possible. Among a multitude of other symptoms he described irises which had "white or very light yellow, clearly defined pinpoints near the outer margin, generally placed at regular intervals in a ring, and appearing to be placed on the iris." He goes on to say that in some cases where these spots were found the follow-up showed that these children developed normally. On the other hand, he found that all mongolian patients had these blue irises and yellowish-white spots. In cases in which the irises changed their color and turned brown, these spots disappeared. In summary he found:

1. All mongols are born with blue irises which show these particular white spots. If the iris changes to brown these spots disappear.

2. Not all children with blue irises and these spots develop into morons, so that these types of irises can be found in adults also.

These white spots on the iris are not as rare as I originally thought. Since I have become interested in them I have seen quite a few blue irises with these particular nodules.

According to Adalbert Fuchs, the anatomic substrate of these white warts is apparently a circumscribed dense accumulation of the anterior layers of the iris stroma, which appear white in blue irises because they are not hidden by the pigment-ladened chromatophores.

SUMMARY

Peripherally situated, elevated, white, wartlike, small spots of the iris are physiologic occurrences. Berliner calls them Krückmann-Wölfflin bodies. Since they are not bodies, it may be better to call them Brushfield spots. All mongolians are born with these spots on blue irises but some babies, who have blue irises with these spots, develop into normal adults.

225 East 79th Street (21).

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MOIST CHAMBER

LESTER L. COVELL, M.D.
Boston, Massachusetts

The use of a moist chamber as a form of therapy in ophthalmology has not been fully appreciated. A survey of American and British literature during the past 10 years is almost devoid of reference to the practicability of such a device. Klein mentioned the use of a contact shell applicator for use in a corneal bath. Ernst Fuchs does prescribe a watchglass attached to the rim of the orbit with adhesive, but the nuisance involved in applying the latter apparatus, with the possible discomfort to the patient, is the probable basis for its lack of popularity.

The importance of moisture and adequate lubrication of the cornea needs no great elaboration. Exposure and diminution of tears are of importance in the etiology of many metabolic and neurotrophic corneal diseases. Patching of the involved eye or tarsorrhaphy are not always expedient. Many of these corneal problems are present in extremely elderly people, and the diminution of tears in patients over 50 years of age has been well established.

Among the corneal problems which can be aided by the use of the moist chamber are keratoconjunctivitis sicca, keratitis associated with lagophthalmos, exophthalmos, and ectropion, as well as for the protection

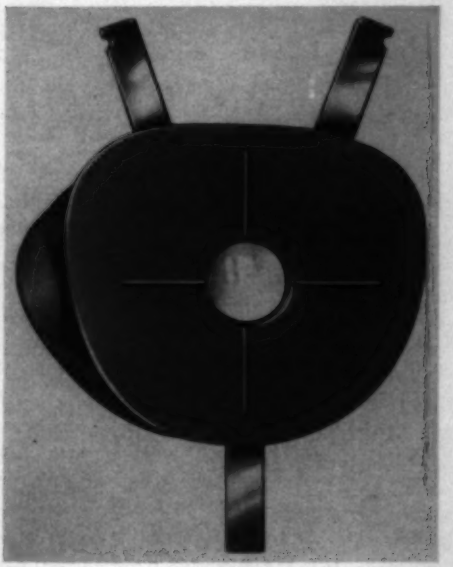

Fig. 1 (Covell). Front view.

Fig. 2 (Covell). Posterior view.

Fig. 3 (Covell). Device in use.

of the cornea in comatose states. Many elderly people are plagued by superficial keratitis-epithelialis of unknown etiology. The neurotrophic type of keratitis associated with injury to the fifth nerve or following surgery to the semilunar ganglion also creates problems which can be alleviated with the use of a moist chamber.

Maumenee recently mentioned the use of a moist chamber as treatment for keratitis secondary to keratinization of the tarsal conjunctiva.

I feel that if a simple prefabricated moist chamber were available to ophthalmologists more use would be made of this device in the supportive treatment of many corneal problems.

With the assistance of the American Optical Company such an apparatus has been prepared. The base consists of a plastic occluder which can be attached to the patient's glasses by means of three malleable prongs. The occluder fits behind the patient's lens and creates an air-tight chamber over the front of the eye. A disc, one cm. in diameter, of transparent plastic material is placed in the center of the occluder so that the patient's vision is unobstructed. On the posterior surface of the occluder a similar disc of absorbent material is placed. This disc can be readily permeated with medication or water. The heat of the eyeball allows the fluid to be evaporated and thus creates adequate moisture and lubrication for the cornea.

This device has now been used in seven cases, in such varying conditions as keratitis-epithelialis, keratoconjunctivitis sicca, corneal dystrophy, and neurotrophic keratitis following injection of the semilunar ganglion caused by tic douloureux. The results have been of sufficient satisfaction to the patient that it is felt that other ophthalmologists might like to make use of this simple apparatus.

Case report

M. L., a 54-year-old white woman, suffered from polycythemia. She complained of impaired

vision with inability to read or enjoy television for any prolonged period of time.

Examination showed visual acuity of 20/50 in the right eye and 20/30 in the left.

Significant findings consisted of multiple punctate opacities involving the epithelium of each cornea. The small punctate areas stained with fluorescein and involved the central area of the cornea, but were more extensive and numerous in the lower half of the corneal surface. A positive Schirmer test was present.

After lack of response to local therapy, including such drops as Neo-cortef (0.5-percent) and methyl cellulose preparations, the patient was given a moist chamber for use at home and also when looking at television.

Visual acuity improved in the right eye to 20/30 and there was a definite diminution of the corneal staining areas. What was more important, from the patient's point of view, was the comfort which ensued while looking at television and movies. Objectively the epithelium of the cornea did not show as extensive staining with fluorescein, although there were still a few irregular staining areas in the lower half of the cornea.

After using the moist chamber for a period of two months the patient was able to discontinue the use of the apparatus for one month without discomfort.

358 Commonwealth Avenue.

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CORNEAL GRAFT TABLE

RUDOLPH BOCK, M.D.
Palo Alto, California

This instrument was designed to minimize the handling of the graft and, in particular, to facilitate the passing of sutures through the graft border before placing it into the recipient cornea bed. This rather delicate procedure requires good fixation of the graft and should be done with as little tissue trauma as possible. A good corneal forceps (Castroviejo or Leahey) can be used to hold the graft but certainly causes more trauma than the one devised by Arruga or Patton which fixes the graft between two shallow cups. With any of these forceps fixation devices the passing of the sutures is done, so to say, in midair.

No carpenter would dream of holding a piece of wood in one hand while cutting it with a saw in the other. We seem so sure of our manual dexterity that we try to do just that when we pass the sutures through the free graft held by a forceps in one hand.

The little table (fig. 1) which I have designed consists of a footplate with interchangeable graft supports for six- to 10-mm.

Fig. 1 (Bock). Corneal graft table.

grafts. The graft can be passed directly from the Franceschetti trephine to the table without being touched, by simply screwing the plunger. As Figure 1 shows, the graft rests about two inches above the foot plate on a smooth convex surface of seven-mm. radius of curvature. A one-mm. high rim, which has narrow openings like battlements at 90-degree intervals, holds the graft (fig. 2). These openings are for the sutures and just wide enough to allow a fine Greishaber corneal needle to pass, therefore, no previous marking of the suture on the graft is necessary and, with a fresh cornea and a

Fig. 2 (Bock). The rim holding the graft.

good needle, the placing of the single-armed sutures is really easy. Soft (older) corneas may require a little counterpressure from above with a Daviel spoon or an iris spatula as the needle enters the graft. The hand holding the needle holder can always remain in the same comfortable and steady position; one simply rotates the table around to pass one suture after the other.

After all four sutures are in place, the graft table is covered by a moistened piece of gauze and is transferred to the instrument table. After the graft bed in the patient's cornea is prepared, one removes the gauze and the graft is lifted by the sutures and transferred to the patient.

145 North California Avenue.

COLLATED NEAR-VISION TEST CARD*

ARTHUR H. KEENEY, M.D.
AND
H. LYLE DUERSON, JR.
Louisville, Kentucky

Evaluation of central visual acuity is remarkably reliable at a distance of six meters in spite of many scientific flaws and variables in the usual clinical methods. Attempts at quantitation in the near range multiply the disturbing effects of these variables and introduce additional uncertainties (size of pupil, accommodative ability, type of distance correction, and others). The Snellen principle of notation, based on visual resolution of a one minute angle, is the sheet-anchor of reference despite both clinical and laboratory methods demonstrating resolving power beyond this in many eyes. Dozens of proper names† speckle the literature with variously practical and impractical figure or letter forms of test objects evolved from the Snellen principle.

In near testing, confusion has been primarily eponymized by the 1854 "Schriftscalen" of Eduard Jaeger which was merely a series of variously sized types selected from materials on hand at the convenience of Jaeger's printer. Reproductions in many languages have shown no consistency even with the original random sizes. Critically designed near cards often have been handicapped by technical difficulties in production (A.M.A., Berens) or necessity for the examiner to look with the patient at the test material (Lebensohn, Guibor).

A practical near card with optimal accuracy should:

1. Be designed from the Snellen principle of a one-minute angle of minimal visual resolution.

* From the University of Louisville, School of Medicine, Section on Ophthalmology.

† Landolt, Reid, E. Fuchs, Kuchler, Smee, Striedingen, Birkhauser, Golvin, Miller, Friedman, Evans, Schweigger, Boettcher, Berens, Hutchinson, Fink, Lebensohn, Guibor, Sloan, Stimson.

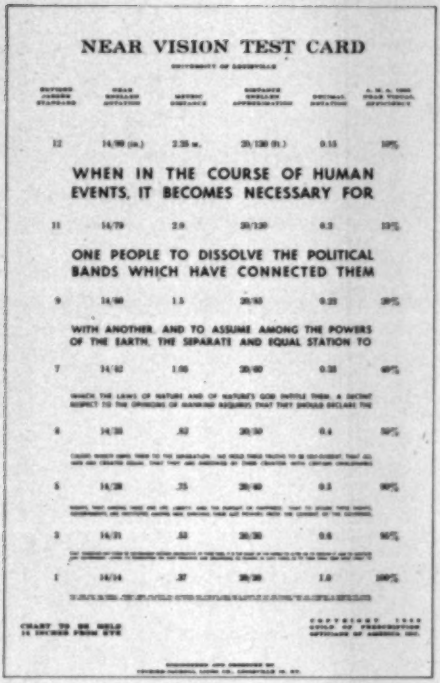
NEAR VISION TEST CARD
WHEN IN THE COURSE OF HUMAN
EVENTS, IT BECOMES NECESSARY FOR
ONE PEOPLE TO DISSOLVE THE POLITICAL
BANDS WHICH HAVE CONNECTED THEM
WITH ANOTHER, AND TO ASSUME AMONG THE POWERS
OF THE EARTH, THE SEPARATE AND EQUAL STATION TO

Fig. 1 (Keeney and Duerson). Front side of collated near vision test card.

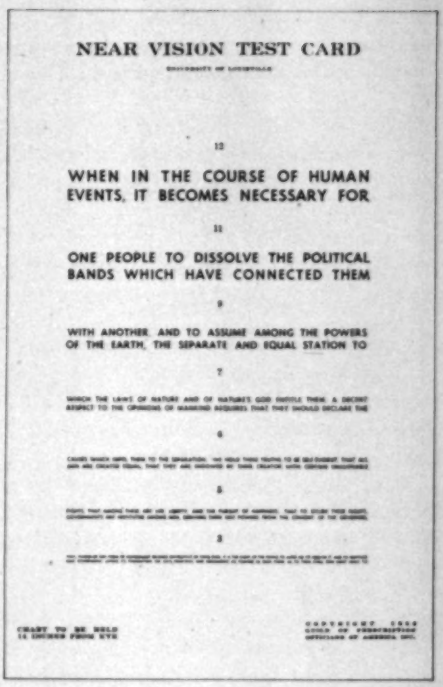

Fig. 2 (Keeney and Duerson). Reverse side of collated near vision test card.

2. Recognize the uncontrollable variables affecting near-vision testing in greater magnitude than these variables affect distant vision.

3. Be rendered in practical sentence structure and familiar word arrangement simulating conventional near tasks.

4. Free the examiner from necessity of looking with the patient at the text.

5. Use mat reflecting or minimal glare surface without heavy coating or plasticizing, yet one with elimination of ink spreading.

6. Avoid letters in various case as well as in ornamental or serif forms.

7. Avoid emotional or strange word material.

8. Indicate and collate major notations used in near acuity.

9. Be widely available and replaceable as an inexpensive, expendable item.

Increasingly specific demands of insurance carriers, compensation boards, and military examinations necessitate more critical quantitation of near acuity. Prompt translation from one notation to another is sometimes needed to meet various requests in these categories.

A new collated near card has been engineered* to meet these considerations, yet to retain practical and workable form. A slight compromise has been made in letter form from the pure box-type letter of Snellen, yielding a letter slightly higher than it is wide, in keeping with commonly used proportions. Extremely critical printing de-

* Pilot model presented September 29, 1955, at the annual meeting of the Eye Section, Kentucky State Medical Association.

mands have been met.* The height of each letter subtends a five-minute minimal visual angle (each component of the letter subtends a one-minute visual angle) at the distance in inches indicated by the "near Snellen notation," assuming 14/14 to be normal or "100 percent" near acuity. Comparable metric distances at which these types should be read are indicated in the nearest, commonly used figures. For continental users, the decimal notation (of Monoyer) is equated usually to the nearest tenth. Because there is no exact equivalent between near and distance Snellen notation, a "distance Snellen *approximation*" is expressed in feet. On the somewhat arbitrary selection of 14/14 (0.37 metric distance; 1.0 decimal notation; 20/20 distance Snellen approximation) as average normal near acuity, a *revised Jaeger standard* (RJS) has been calculated and should be indicated not merely as "Jaeger type" but as "RJS."

The A.M.A. "near visual efficiency" percentages as revised in 1955 are appended in nearest round numbers. These percentages are empirical but are included because they have achieved a measure of legal acceptance in some states.

For any standard to be widely understood and accepted, it must be widely available. A valuable service has been performed by the members of the Guild of Prescription Opticians of America who have underwritten the development of this collated card. The Guild is further undertaking to distribute the card to all physicians performing eye examinations. Such widespread availability of this standard with its collation of various notations should go far to reduce confusion in expressions of near visual acuity.

1406 Heyburn Building (2).

* By Mr. Morris Davidson, Courier-Journal Litho Company, Louisville 18, Kentucky.

SUPPLEMENTAL INTRAVENOUS ANALGESIA*

For cataract surgery

Frederick D. Williams, M.D.
Stamford, Connecticut

The purpose of this preliminary report is to emphasize a method of analgesia for ocular surgery. Continuous intravenous analgesia was proposed by the Stamford Anesthesia Associates in 1956, and has been used for 100 patients.[1] Ophthalmic surgeons in Great Britain have advocated it and it has been used on this continent for obstetrical and general surgery.[2-8]

In cataract surgery premedication consists of promethazine (Phenergan) hydrochloride (25 to 50 mg. orally) and usually secobarbital (Seconal, 100 mg.) at night.

Phenergan (25 to 50 mg.) is given intramuscularly two hours before operation. Meperidine (Demerol) hydrochloride (25 to 100 mg.) and scopolamine or atropine (0.3 to 0.4 mg.) are given one hour before operation—dosage varying with weight and age. Demerol (250 mg. in 500 cc. of saline (0.05 percent) is injected intravenously several minutes before local anesthesia and akinesia are given. Akinesia and local anesthesia are obtained by a modified O'Brien technique and a retrobulbar injection, using lidocaine (Xylocaine) hydrochloride (two percent), hyaluronidase (Wydase, six to 10 turbidity units per cc.), and adrenalin (1:50,000).

Digital pressure on the globe and occasional lidocaine additional akinesia for the rectus muscles complete the preoperative measures.[9] During operation intravenous Demerol (0.05-percent solution) is continued and intravenous Phenergan (12.5 to 50 mg.) is used, if necessary, to reduce apprehension.[10] After closing the incision, the need for medication generally ceases. This procedure can be used with some changes for plastic, glaucoma, and detachment surgery.

* From the Ophthalmology Service, Department of Surgery, Stamford and Saint Joseph's Hospitals.

This type of supplemental analgesia produces a quiet and co-operative patient who notes only minor annoyances of dryness of the mouth and occasional itching. Blood pressure, pulse, and respiratory rates remain stable, except in some patients whose blood pressure is over 160 systolic. In these patients a decrease of 30 mm. Hg systolic and 10 mm. Hg diastolic is noted. There is no central nervous system stimulation.[11]

One patient had a mild, short-lived basilic phlebitis. Another patient became hypoxic. Oxygen given by the anesthetist soon restored normal respiration. When Demerol was combined with an intravenous barbiturate, a 79-year-old man exhibited disorientation which was absent when the procedure was repeated later without a barbiturate.

The average amount of Demerol used is 143 mg., including premedication. The maximum amount is 275 mg., and the minimum is 25 mg. The average amount of Phenergan is 43 mg., including premedication. Maximum and minimum amounts are 75 and 12.5 mg.

This method offers a gradual flexible control of analgesia and sedation which can be easily adjusted to varied surgical procedures and to each patient's requirements. In contrast to Demerol used for abdominal and thoracic surgery, we find that increasing the rate of flow does give adequately rapid adjustment in the degree of analgesia.[6] Transient restlessness and anxiety can be quickly overcome. Avoidance of pain during the procedure depends upon experienced anticipation of pain-producing steps during surgery. It must be kept in mind that a wide range of dosage will result in the same desirable effect in different individuals.

Postoperative recovery room supervision may often be avoided because the patient is awake and co-operative on leaving the operating room. On arrival to the hospital room the patient's alertness reduces nursing attention and the need for restraints. Barbiturate-induced mental and physical disturbance is not present.

With the slow, diluted administration of Demerol in the supine position, peak dosage leading to circulatory and respiratory depression is avoided.[12] Furthermore, the surgeon's relaxation and freedom to converse are maintained, and gastrointestinal disorders are greatly reduced.[13] Frequent observation of vital signs by an anesthetist during operation is particularly helpful for patients of higher-than-average risk.

The gradually increasing sedation, absence of pain during operation, and comfortable recovery period help patients to look forward with confidence to a cataract operation on their second eye. The additional expense and possible phlebitis are minor disadvantages.

Summary

A method is given for supplemental analgesia which appears to offer flexible and careful patient control in cataract surgery. Ability to obtain satisfactory local motor and sensory block is essential.

Evaluation after more experience with this method will be necessary to establish its merit.

1 Atlantic Street.

I am greatly indebted to Dr. Frank D'Andrea, for his proposal of this method, and to Dr. Newell W. Giles, for permission to include his patients in this series.

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TUBOCURARINE AND NEMBUTAL ANESTHESIA*

IN RABBIT EYE SURGERY

WAYNE COLLINS, D.V.M.
L. BYERLY HOLT, M.D.
AND
KATHRYN ROBESON, B.S.
Winston-Salem, North Carolina

After one rabbit in four died from anesthesia either preoperatively, during operation, or postoperatively, new techniques were carefully developed in anesthesia in 100 rabbits.

EQUIPMENT USED

The following equipment was used for rabbit eye surgery of corneal transplantation: pediatric scales, 25-gauge needles, 10-ml. glass syringes, Hagler's tongue forceps (to clamp ears), 20-ml. bottles of Abbott's Nembutal, 10-ml. bottles of E. R. Squibb's Tubocurarine, 50-ml. bottles of saline, a Grant and Trotter rabbit holder (developed at the Massachusetts Eye and Ear Infirmary in Boston), and 11-pound New Zealand White, California White, Flemish Giant, and Himalaya rabbits.

PROCEDURE

The rabbit was weighed on a pediatric scale.

The rabbit was placed in a Grant and Trotter rabbit holder. The fur on the rabbit's ear was cut short with scissors and moistened with alcohol, or Zephiran. Shaving the fur caused the blood vessel to constrict. A Hagler tongue forceps was placed on the blood vessel at the base of the ear of the rabbit. The 25-gauge needle was placed parallel to the blood vessel, with the bevel (slanting point) next to the blood vessel; it was then inserted directly into the blood vessel. Two-tenths ml. Nembutal, and two units of Tubocurarine for each pound were slowly injected with a 25-gauge needle over a period of five minutes.

The corneal reflex was tested by dropping sterile saline on the rabbit's cornea. The eyelid reflexes were tested by touching the eyelids with sterile cotton applicator sticks. After the eyelid reflex is abolished, the rabbit is not disturbed from a comfortable stretched-out, prone position for eight to 10 minutes. This allows the anesthesia to become more complete for intraocular eye surgery and permits the rabbit to adjust to the anesthesia. One or two drops of one-half percent tetracaine is dropped on the cornea.

The toes of the rabbit were bent upward, placing the tendons on a stretch, causing a reflex action if the anesthesia were not deep enough for surgery.

If the anesthesia is not deep enough, the Tubocurarine and Nembutal are continued until the rabbit is ready for surgery. Additional anesthesia is usually not necessary during operation but can be given if necessary.

This method of anesthesia gives the deep relaxation necessary for intraocular surgery and helps to prevent anesthetic death.

209 Reynolds Building.

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* From the Marguerite Barr Moon Eye Research Foundation, Inc. This study was aided by a grant from The National Institute of Health, Bethesda, Maryland, under contract No. B-1243.

SOCIETY PROCEEDINGS

Edited by DONALD J. LYLE, M.D.

NEW ENGLAND OPHTHALMOLOGICAL SOCIETY

438th meeting, November 20, 1957

VIRGIL G. CASTEN, M.D., *presiding*

INTERESTING PEDIATRIC SYNDROMES

SUMNER D. LEIBMAN, M.D., Boston, Massachusetts:

In the first syndrome the patient was a three-year-old boy. The ocular findings were bilateral ptosis with little or no levator function in either eye with the margin of the upper lid slightly below the visual axis of the right eye and slightly above that of the left. There was thought to be an inverted epicanthic fold of both eyes, more on the right than on the left. There was an entropion on the right with the lashes impinging on the lower cornea. The cornea was undamaged. The extraocular muscles, pupils, media, and fundi were normal. Both eyes had a moderate compound hyperopic astigmatism. The child tilted his head backward in the usual fashion to compensate for the ptosis. The brow ridges were so flat as to appear almost absent. There seemed to be a little effort made by the frontalis to elevate the lids.

The skin of the face appeared puffy and edematous. The ears were small, misshapen, and placed low on the head. There was obvious misalignment of the teeth. The neck was huge.

Consultation with the pediatrician brought out the fact that the child had the Bonnevie-Ullrich syndrome. The classic features of this syndrome are: Webbing of the neck, deep-set ears, high-arched palate, lymphangiectatic edema, sagging eyelids, low hairline at nape of neck, short stature, cubitus valgus, sexual infantilism, hypoplasia of the nipples, short, spoon-shaped toes and nails, and a predilection for females. There is no acceptable pathogenesis of these conditions.

This patient underwent a Reese orbicularis sling ptosis operation. At first the results were good but gradually the effect was lost. The boy seems to be slightly retarded mentally and it has not been possible to determine his visual acuity accurately. However, he has been fitted with glasses. At present it is planned to correct the entropion of the lower lid of the right eye. Attempts will be made in the future to correct the ptosis.

The second interesting pediatric syndrome is the one that has become known as the Riley-Day syndrome. The principal ocular findings of this syndrome are alacrimia (child cries without tears), corneal hypesthesia or anesthesia, keratopathy which may or may not be present, if it is present it may be a severe keratomalacic type characterized by indolent diffuse opacification of the stroma, keratinization and sloughing of the epithelium, white eyes with anesthetic corneas, and usually bilateral.

The absence of tears and the presence of the rest of the clinical picture are necessary to make an accurate diagnosis.

Tarsorrhaphy should be done as early as possible. Permanent scarring usually occurs and perforation is a great danger.

There is a less serious superficial ulceration of the lower cornea which may be due to exposure or dehydration of the cornea which responds rapidly and readily even to the mere instillation of saline drops; however, a bland ointment might be better.

There may be no obvious keratitis but slit-lamp examination may reveal multiple punctate opacities or more diffuse etching of the lower cornea.

These children seem to have a sympathetic nervous system which is disordered. Other features of the syndrome are bouts of hyperthermia, bouts of fever, dehydration, sweat-

ing, postural hypotension, hyporeflexia, drooling, tongue biting. The patients are usually Jewish.

Surgical treatment of scleromalacia perforans

Malcolm W. Bick, M.D., Springfield, Massachusetts:

The patient, a 60-year-old man, had a noncontributory past history except that in 1945 he had developed a severe arthritis of the feet which progressed rapidly and eventually involved other joints. By 1955 he had become bedridden.

Three months prior to being seen by me in 1956 he developed a small reddish nodule on the inferior nasal aspect of the left eye and this nodule rapidly grew in size until there was a scleromalacia process that involved the entire nasal quadrant of the eye. The superior portion of the globe was disease free. From the 10-o'clock to the 6-o'clock positions on the cornea, there was an area where several small vessels arborized.

It was elected to try to cover in some way the area of the scleromalacia. A conjunctival incision was made well back of the fornix and thus preserved as large a flap as possible. The conjunctiva was not cut away, it was reflected. An island of intact conjunctiva on the temporal side was left in place. The four rectus muscles were exposed. With great care an intact conjunctival flap was reflected back toward the cornea to reveal the mass of bulging uveal tissue. This uveal tissue was then cauterized. It was reasoned that this would cause the mass to shrink and that there would also be an inflammatory reaction that would make the uveal tissue more adherent to the new tissue that was to be introduced.

A piece of fascia lata which had previously been removed from the patient's thigh was fashioned to conform to the circumference of the involved sclera. To obtain firm adherence this large transplant was attached at the insertion of each of the recti muscles with two mattress sutures each. To prevent the graft from sliding forward on the globe, many fine sutures were placed where there was fairly solid sclera.

The eye was dressed with terramycin ointment every second or third day and the patient was discharged from the hospital at the end of the third week. At that time the conjunctiva was pretty well healed over, a continuous conjunctival flap had developed, and the corneal edema was still present to a certain extent.

One interesting postoperative development was the appearance of heterochromia: the eye which had been brown began to become a little blue.

The patient's preoperative vision had been 10/200 with a lot of corneal edema and a tremendous distortion of the cornea. At four months postoperative the patient's vision was correctible to 20/20−1 and he maintained this vision to the end. The patient died seven months after operation.

Discussion. Dr. F. H. Verhoeff: Why did you use so much fascia lata? Why not confine it to the smallest area and then if necessary do it again if a new break-through developed? Those results of yours are very interesting and remarkable, but I think it would work just as well if you used only a flap. Why wouldn't that be enough? That's what I would have tried and maybe it's lucky I didn't have the case.

Dr. Trygve Gundersen: It seems to me that fascia lata is not a very satisfactory material for this purpose. I have had some experience with it and I find that it stretches and if there is any pressure behind it it thins out and in two or three years' time you don't know if you have any fascia lata there. Wouldn't it be better to use or try to use sclera from the "sclera bank"?

Dr. Malcolm W. Bick: According to the literature there have been two cases in which scleral grafts were used and those cases failed. In our case it seemed extremely difficult to make and attach a scleral graft for the highly irregular series of perforating nodules we had. We used a heavy, dense piece

of fascia lata obtained for us by an orthopedic surgeon and we used the size we did because we wanted to be able to fasten it to firm tissue. The graft had to be big to do this.

Charles Snyder,
Recorder.

COLLEGE OF PHYSICIANS OF PHILADELPHIA

Section on Ophthalmology

December 19, 1957

I. S. Tassman, M.D., *Chairman*

Filaria loa

R. D. Harley, M.D., Atlantic City, New Jersey (by invitation):

Loa loa, a filaria indigenous to West Africa, is rarely encountered by ophthalmologists in this country. This fact together with the dramatic appearance of the worm beneath the conjunctiva is of interest and deserves comment.

A woman missionary nurse was seen June 9, 1957, because of a recurrent episode of a worm in the left eye. She had recently come from the Belgian Congo where Loa loa was prevalent. She had been bitten by a Mangrove fly (Chrysops) in 1948. Her first symptoms of the worm's presence were in the form of migratory calabar swellings in 1951. The patient's rest had been disturbed the entire night of June 8th by the movements of the filaria in the left eye. Upon examination the next morning it was plainly visible undulating over the sclera in the subconjunctival space. The worm was removed from the subcutaneous tissue of the left lower lid after an unsuccessful attempt to extract it from the subconjunctival space. Brief descriptions of the intermediary host, the mangrove fly, and the parasite, Filaria loa, were presented. The most effective treatment is surgical extraction of the adult worm. A suggested technique for the removal of the filaria was outlined.

Superficial keratitis due to plastic foreign bodies

T. D. Duane, M.D. (by invitation):

Approximately 75 cases of keratitis due to the presence of small flakes of bouffant (modified nylon) on the superficial epithelium of the cornea were described. The flakes which appear as a result of shearing of the stiff plastic material are chemically inert and produce low-grade symptoms due to their mechanical foreign body attributes. They are difficult if not impossible to see without biomicroscopic magnification and can best be removed by lifting them away with a spud or needle. Dr. Duane's experiences have been confined chiefly to garment workers but more recently cases have appeared among the general populace. He warned that similar instances may appear as the material is more widely used in clothing and household decorations. Typical cases were presented.

Use of Tenon's capsule in strabismus surgery

Francis Heed Adler, M.D.:

Strips of Tenon's capsule may be used to pull the eyes into alignment where an ocular muscle has been cut accidentally or is congenitally absent. In three cases this has proved to be a simple and effective measure resulting in good alignment of the eyes, and in two of the cases complete restoration of ocular motility. This was due presumably to the inclusion of muscle fibers in the tongue of Tenon's capsule.

The paper was published in full in The American Journal of Ophthalmology in the issue dedicated to Sir Stewart Duke-Elder. (May, 1958, Part II).

William E. Krewson, 3rd,
Clerk.

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PREVENTION OF ANGLE-CLOSURE GLAUCOMA

More and more people seem to come to us for routine examination stating that they want to be sure that they have healthy eyes and often specifically mentioning that they want to be sure that they do not have glaucoma. In examining such patients in the usual fashion and finding normal vision, slitlamp findings, and normal fundi and tonometer readings, we assure them that their eyes are entirely healthy. But if any of these patients develop angle-closure glaucoma in the near future, how far does our responsibility go in this matter? A shallow anterior chamber is so easily recognized that should not we as medical doctors at once rule out the possibility of angle-closure glaucoma is every such case? The understanding of the mechanism of angle-closure glaucoma and its pre-

vention by peripheral iridectomy are generally accepted so it would seem that it is our duty never to permit a case of such glaucoma to develop.

This presumes at once that we have strong convictions on the subject, but don't we all have strong convictions about the use of smallpox vaccine, for example? It might be argued that the risk of the use of vaccine is small as compared to an intraocular operation. However, one merely has to remember a few examples of eyes blinded from needless angle-closure glaucoma to get the right perspective. I think most of us will agree that peripheral iridectomy is here to stay.

In my own private practice I do a gonioscopic examination at the slitlamp in every case of shallow anterior chamber. This may sound formidable but it actually takes only a few moments. One need not be an expert to recognize whether the angle approach is dangerously narrow or that there are peripheral anterior synechias. The intraocular pressure is taken routinely with a tonometer but, in these cases, unless there is actual closure or a chronic simple glaucoma, the pressure will be well within normal limits.

I then refer the patients with extremely narrow angles to the tonography department at the Washington University Medical School. It goes without saying that it is easy for us who have such excellent facilities to have provocative tests made, but the darkroom and dilatation test can be done as an office procedure, of course. I give the patient a prescription for two-percent pilocarpine, which is presented to the technician in the tonography department for use when the examination is completed. The laboratory examination consists of a tonogram, followed by Euphthalmine dilatation of the right pupil, followed by a second tonogram.

In the average positive result the outflow will be diminished by more than 25 percent. The intraocular pressure very well may not have risen in this short time but it is believed by most of us here in Saint Louis that an impairment of the outflow of this degree is conclusive evidence that angle-closure glaucoma can take place in such an eye. The technician now uses the pilocarpine two or three times in the right eye and then sends the patient home. The patient has already been instructed by me and reminded by the technician to continue the use of the pilocarpine every hour for the rest of that day until bedtime. (As the reader might suspect one of my patients developed an attack of acute angle-closure glaucoma the night of the test hence this prolonged use of the pilocarpine.)

A comprehensive study on this entire subject by Bernard Becker appears in the September, 1958, issue of THE JOURNAL.* The reader is referred to this very excellent article which gives an analysis of a large series of such cases. This type of glaucoma seems to be sufficiently clear cut that we all should be very familiar with its recognition and care. This article adds much to our understanding.

The results of such a routine in my own cases have been approximately one positive case in five. My own feeling in regard to my patients is that this positive provocative test in the presence of the extremely narrow angle is indication enough for peripheral iridectomy.

The cases with negative provocative tests should be watched over the years, for with aging the angle will become narrower, of course. I never recommend iridectomy unless there is definite evidence that angle-closure can take place. As an example of this side of the problem, I have in mind a brother and sister in their fifties each of whom has extremely narrow angles when seen gonioscopically but the provocative tests have been negative. Their elderly mother lost an eye several years ago from a neglected angle-closure glaucoma, and she has an extremely narrow angle in the other eye. I am certain that the time will come when this brother and

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* Becker, B., and Thompson, H. E.: Tonography and angle-closure glaucoma. Diagnosis and Therapy. Am. J. Ophth., **46**:305 (Sept. Pt. I) 1958.

sister will be candidates for peripheral iridectomy. Fortunately, they are both very intelligent and quite understanding of the condition and willing to have the provocative tests repeated at intervals. It hardly seems necessary to add that an attack of angle-closure glaucoma in one eye would be the strongest possible indication for peripheral iridectomy in the other eye.

There will be some surgeons who are unwilling to recommend an intraocular operation for persons who have never had an attack of acute angle-closure glaucoma. With Diamox and strong miotics it is true that many eyes can be brought out of an acute attack without permanent damage to the optic nerve and no impairment to outflow. Statistically we know, however, that sooner or later many of these eyes will have an attack of angle-closure glaucoma in spite of the use of miotics. At this point may I add my condemnation to the continued use of Diamox in such cases. Chandler and others have written so clearly on this subject that no one should have any misunderstanding. The severe acute attacks may be controlled but milder ones may occur, with increasing synchias and permanent impairment to outflow.

Many ophthalmologists believe that by explaining carefully to their patients the nature of an acute attack with its symptoms of blurring and redness and halos that these people will get in touch with us promptly and treatment can be instituted in time to avoid a dangerous attack. In my own experience, however, I have seen a number of eyes in the state of acute glaucoma with little or no symptoms. The disease is not always so dramatic. I have in mind a nurse who had been fully informed by me some time ago that she might have such an attack. Recently she came to my office to have her eyes tested so that she could get some sunglasses for a trip abroad. She was absolutely symptom free with normal vision but, when I examined her at the slitlamp, the iris was in contact with the cornea, and the tonometer reading was off the scale. There was absolutely no redness of the eyes whatever. The condition was bilateral. In several other instances of eyes that were lost, the symptoms were only slight redness and rather vague pain described by the family doctors as "a cold in the eye."

The operation of peripheral iridectomy is not a completely innocuous procedure. Several years ago, by faulty technique, I caused a traumatic cataract. The modern procedure wherein the iris bulges out of the scratch incision is nearly free from such danger for no instrument enters the eye, and the anterior chamber is not even lost. However, I recently had one patient who developed a hemorrhage in the anterior chamber on the fourth postoperative day. The operation had been completely uneventful and the patient most co-operative. The clot completely disappeared without complications.

In summary, this problem presents itself as this: angle-closure glaucoma may be anticipated and prevented. Shouldn't we as eye surgeons face up to the situation and never permit angle closure to occur? If we are wholeheartedly enthusiastic about the diagnostic procedure and the merits of the operation and have confidence in our own surgical ability, we can impart this feeling to our patients. True, we are taking on a grave responsibility for, after all, such an eye in a sense is a perfectly normal one: but the deepened anterior chamber resulting from the operation not only affords security to the patient but gives objective proof of a job well done.

H. Rommel Hildreth.

ITALIAN OPHTHALMOLOGY

Ophthalmic journalism in Italy began 100 years ago with the founding of the *Giornale d'Oftalmologia Italiano-Stati Sardi* (Journal of Ophthalmology of Italy and Sardinian States) by Borelli in 1858 which continued publication till 1869. G. B. Borelli (1813-1891) was an associate professor at the Turin University Medical School, whose

broad interests included ophthalmology though he did not specialize in this field. Previously, in 1850, he had founded a journal of general medicine. The oldest of the extant ophthalmic journals now published in Italy is the *Annali di Ottalmologia e Clinica Oculistica* (Parma), founded in 1917 through union of the *Annali di Oftalmologia*, established by Quaglino in 1871, and the *Clinica Oculistica*, established by Cirincione in 1889. Five other prewar ophthalmic journals continue publication. These are:

Archivio di Ottalmologia (Naples). Bimonthly, founded in 1893, now edited by Sgrosso.

Atti della Societá Oftalmologica Italiana. Established in 1924.

Bollettino d'Oculistica (Florence). Monthly, founded in 1922, now edited by G. B. Bietti.

Rassegna Italiana d'Ottalmologia (Turin). Bimonthly, founded in 1932, now edited by Gallenga.

Rivista Oto-neuro-oftalmologica (Bologna). Bimonthly, founded in 1923, now edited by Caramazza.

Another five periodicals were established since World War II. These are:

Aggioramenti di Terapia Oftalmologica (Pisa). Bimonthly. Edited by Cattaneo.

Annata Terapeutica in Oftalmologia (Pisa). Italian translation of the French annual of similar name.

Atti della Societá Oftalmologica Lombarda (Milan).

Giornale Italiano di Oftalmologia (Florence). Bimonthly, now edited by Rubino.

Rivista Italiana del Tracoma e di Patologia Oculare Virale ed Esotica (Catania). Quarterly, edited by Favaloro.

Italy is a country with a great tradition of teachers and scholars. It emerged from the losses of World War II with a fatalistic endurance that seems to be its characteristic attribute. The stamina and vigor of Italian ophthalomology are indicated by the surprising innovations that have emerged. Among the more familiar are the Maggiore perimeter and the anterior chamber acrylic lens.

A by-product of the scientific renaissance, which incidentally trailed the literary renaissance by two centuries, was the organization of academies such as the Accademia della Crusca, Florence, 1582, and the Accademia dei Lincei, Rome, 1603. Among the members interested in eye problems were Grimaldi (1613-1662) who demonstrated diffraction, and Porta (1538-1615) who invented the camera obscura. The last of this group was possibly Massaria, a die-hard Galenist, who wrote in 1669 that it was better to err with Galen than to be right with the moderns.

University instruction in ophthalmology started in the 18th century. Scarpa, who taught at Pavia, wrote a classic text. Buzzi antedated Soemmerring in recognizing the macula lutea. Fontana was the first to observe that the pupil contracts during sleep. Valsalva, a pupil of Malpighi and the teacher of Morgagni, noted that the lens increases in size with age. Baglivi was the first to distinguish between smooth and striped muscle (1710) and Ramazzini initiated the study of occupational hazards and industrial hygiene (1739).

The introduction of the ophthalmoscope, asepsis, and anesthesia in the second half of the 19th century effected a blossoming of ophthalmology in Italy, as elsewhere. Quaglino published an atlas of ophthalmoscopy. Manfredi, in collaboration with Golgi, studied the retina (1872). In 1879, the Italian Ophthalmological Society was founded. De Vincentiis suggested goniotomy in 1892, a procedure widely accepted for congenital glaucoma since its elaboration by Barkan. Toti of Florence originated the modern operation of dacryocystorhinostomy (1904), which in an improved form has now generally supplanted dacryocystectomy. Reymond, an authority on physiologic optics, wrote on the determination of angle alpha (1905). The otologist, Giuseppi Gradenigo (not to be confused with the distinguished ophthalmologist, Pietro Gradenigo), detected the paralysis of the lateral rectus that

occasionally complicates acute mastoiditis. Notable ophthalmic contributions were made in bacteriology by A. Bietti and Cavara, in ocular physiology by Angelucci, in histology of the retina by Pacini and Tartuferi, in microscopic pathology by De Vincentiis, C. Gallenga, and A. Bietti, in embryology by Cirincione, and in the history of ophthalmology by Puccinotti and Ovio.

At present Italy has 21 university ophthalmic clinics, all state supported. The major institutions are in Rome, Naples, Genoa, Florence, Bologna, Milan, and Turin. Independent ophthalmic services exist also in the same cities and in Venice, Trieste, Brescia, and many other minor cities. Original surgical contributions frequently emanate from these independent services, such as the anterior chamber acrylic lens, conceived by Strampelli of Rome in 1954. The university clinics have facilities for clinical research but specialized investigation requires the facilities of the university institutes. Research is handicapped by insufficient funds; some directors, however, have surmounted this difficulty through personal efforts at fund raising. Prof. G. B. Bietti has by this means made his clinic at Rome one of the best equipped in Europe. The current research projects of some of the professors of ophthalmology are: Cattaneo of Milan, retinal circulation; Maggiore of Genoa, physiologic optics; Lo Cascio of Naples, metabolism of ocular tissues; Bietti of Rome, chemotherapy and virus diseases.

In Italy, as in Europe generally, streak retinoscopy is still a novelty but indirect ophthalmoscopy and ophthalmodynamometry are utilized more than in the United States. The detailed treatises most in use are the three-volume work on ophthalmology by A. Bietti and the just completed four-volume work on ocular surgery by Leonardi. Recent important monographs are on ophthalmoangioscopy by Gattaneo, ocular dioptrics by Lo Cascio, ocular mycosis and ocular herpes by Cavara, virus infections by Cavara and G. B. Bietti, vitamins by G. B. Bietti, ocular muscle paralyses by Focosi, and an atlas of ophthalmoscopy by Di Marzio.

Italian medical schools are open to all, regardless of number. The new Italian constitution—which recently celebrated its 10th anniversary—guarantees to all deserving young people the right to study. The gaining of knowledge is an individual challenge and there is no compulsion to follow the courses and lectures. The legend of the Renaissance as typified by Leonardo da Vinci, whose interests encompassed art, science, and the humanities, dominates the Italian student. The conscientious student strives to be well prepared both culturally and technically. The ophthalmic services in the hospitals are run by qualified salaried assistants under a director in charge. Residents are considered under instruction and are therefore not paid. The assistants receive a minimum stipend of $100 monthly, which is not enough, even allowing for the lower cost of living in Italy. Now that reconstruction has been completed, better financial arrangements may be expected.

When the idea of this commemorative editorial came to mind, I remembered reading an interesting case study (Arch. Ophth. 57:454-456 [Mar.] 1957) by Bruno Bagolini, formerly senior resident, Ophthalmic Service, Boston City Hospital, and now assistant at the University Eye Clinic at Rome directed by Prof. G. B. Bietti. I solicited his co-operation which he has given fully despite his own many activities. I have relied on him for all the data and for much of the comment. He is highly conscious of Italian history and creativity and in his own career has sustained his people's tradition. Though only three years have elapsed since he qualified in ophthalmology, he recently contributed two additional papers based on his continuing research on motility problems and binocular vision, in connection with which he studied the practices in Germany and Switzerland. He has also achieved the coveted *Libera Docenza* certification which confers a status equivalent to the German *Privat Dozent*. As

long as young ophthalmologists of this type are being developed, Italian ophthalmology may be confident of gifted leaders for the future.

James E. Lebensohn.

CORRESPONDENCE

Recollections of Lawrence T. Post

Larry Post was in the class below me at the Hopkins Medical School so that I never got to know him very well as a medical student. In the years that followed our respective graduations, our paths diverged widely so that there was no opportunity for me to get to know him better. Then, in 1917, came World War I and on May 19th of that year we met again, this time on a steamship bound for France.

Both of us had become members of the St. Louis Base Hospital Unit No. 21, an American Army unit which had been assigned to the British Expeditionary Force and was en route to take over a general hospital of that Force located at a large British base just outside Rouen in Normandy.

It was my good fortune to sit next to Larry at table on the ship and later, on our arrival at our destination, to be assigned to the same tent with him in the officers' compound of the hospital. Under the circumstances it is not surprising that a somewhat remote acquaintanceship beginning in medical school days should develop into an abiding friendship even though our paths were later on to divide once more.

So it is that today my most vivid recollection of Larry Post is concerned with the days when, as junior officers of the American Army unit which took over and ran No. 12 General Hospital of the British Expeditionary Force in France in 1917-1918, we worked hard at our professional duties when occasion demanded, and played just as hard when the work was slack.

I like to recall our walks together into the beautiful forest near the hospital, the innumerable games of bridge which we played in the officers' mess in the evening after dinner, the excursions to nearby Rouen in search of a good French meal and a bottle of good French wine, and of the occasional gay party in the mess to celebrate some American holiday. In all of these doings of the group Larry entered with full zest, just as he carried his full share of the work which the unit was called upon to do.

For me, then, the memory of Larry Post which I cherish most of all is that of a gay and lovable war-time companion whom it is my great good fortune to have known intimately for a time, and to be able to claim as a friend.

(Signed) Alan M. Chesney,
Baltimore, Maryland.

BOOK REVIEWS

Ophthalmic Plastic Surgery. By Sidney A. Fox, M.D. New York, Grune and Stratton, 1958. Second revised edition. 318 pages, 149 illustrations, index. Price: $15.00.

Dr. Fox is associate clinical professor of ophthalmology, New York University Post-Graduate Medical School, and is widely known for his work, especially in reconstructive surgery as it pertains to ophthalmology. The first edition of his book appeared in 1952 and was well received, as evidenced by the need for a new edition six years later.

The second edition is enlarged, parts of it rewritten, and new and better illustrations either were substituted or added. The author adhers to his principle of only including and discussing fully those techniques and procedures with which he is familiar, although he notes exceptions to this principle on occasion.

The result is a most excellent work, remarkably well illustrated, a feature that is not often found in texts on reconstructive surgery, for some strange reason. It is authoritative and most useful.

Derrick Vail.

CONTRIBUTIONS TO THE HISTORY OF OPHTHALMOLOGY. By M. Amsler, Zürich, H. Arruga, Barcelona, F. Berg, Uppsala, Stewart Duke-Elder, London, R. Onfray, Paris, G. Ovio, Rome, A. Pillat, Vienna, F. Rintelen, Basel, W. P. C. Zeeman, Amsterdam. Supplement to Volume 134, Ophthalmologica. Basel, New York, S. Karger, 1957. 119 pages, six figures. Price: sFr. 15.60.

This pamphlet is dedicated to A. Brückner, the editor-in-chief of *Ophthalmologica*, on the occasion of his 80th birthday. It would be difficult to imagine a more appropriate birthday gift than these nine vignettes—each one a gem of its kind.

Amsler contributes a very original "ophthalmologic pedigree" listing all the occupants of the chairs of ophthalmology at the Universities of Bern, Lausanne, Zürich, Basel, and Geneva. Solid arrows indicate "dominant traits," that is, a direct master-disciple relationship or at least a strong influence on the "descendant." Broken arrows mark "mutations," that is, a change to another university. The latter are rare instances —proof that such migrations are rare occurrences in Switzerland.

Arruga traces the history of ophthalmology in Spain back to its Arabic influences. The first textbook to appear in Spanish was written by Domingo Vidál in 1785. The first Spanish ophthalmologic periodical, *Archivos de Oftalmología Hispanos-Americanos*, appeared in 1901 under a truly international editorial staff. Among other publications, it contained an article on the structure of the chiasm by Ramón y Cajal. There follows a brief list of the national and local ophthalmologic societies, the present occupants of the chairs of ophthalmology, and some of the most important recent books on ophthalmology published in Spain.

Berg's approach is quite unique: he selects one facet of the history of ophthalmology in Sweden. Three of the leading surgeons interested in ophthalmology in the Sweden of the mid-18th century all had studied with Johann Ludwig Hommel, an anatomist in Strasbourg. He then goes on to prove in a delightful dissertation that Hommel and not Haller, as is usually stated, should be credited with recognizing the true nature of the vortex veins.

It is obvious from Duke-Elder's history of ophthalmology in Britain that the early milestones were in the theoretic and not the clinical field. Robert Grosseteste, Roger Bacon, and John de Peckhams contributed to optics as early as the 12th and 13th centuries; Newton published his epochal work on reflections, refractions, inflections, and colors of light in 1704—years before Chevalier Tayler gained notoriety as the roving oculist of Europe. British ophthalmology came of age only some 150 years later with the founding of 52 special eye hospitals, 23 of which have survived to this day. The first, and still the greatest, was Moorfield's Hospital founded by John Cunningham Saunders in 1805. It must have been great satisfaction to Sir Stewart to list such names as William Bowman, Jonathan Hutchinson, Warren Tay, Argyll Robertson, and Robert Doyne as his compatriots. Since the end of World War II the picture has changed: it is not the lone research student but a group of scientists that carries on the great tradition in research centers connected with universities. With self-effacing modesty, Duke-Elder fails to mention how instrumental he has been in this development.

René Onfray, in his opening sentence on the history of French ophthalmology, remarks that before the discovery of the ophthalmoscope, ophthalmology was a synonym for a conglomeration of diseases which had in common that neither the patient nor the physician could see clearly. In his lengthy dissertation, he treats the pre-ophthalmoscope era rather briefly. It should be noted that Jacques Daviel presented a series of 206 cataract extractions before the Académie de Chirurgie in 1752; 182 of these cases were considered successful, an enviable record indeed! It is amusing to read that Louis XV

created the first chair of ophthalmology in 1765. He became interested in the subject after he attended an operation on a deer by Daviel. In the second half of the last century three foreigners—de Wecker, Galezowski, and Landolt—made great contributions to the cause of ophthalmology in France. But there is hardly a branch in ophthalmology in which Frenchmen have not done original work or contributed original ideas to known principles. Dupuy-Dutemps, and Bourget created the principle of dacryocystorhinostomy. The name of Morax is synonymous with the bacteriology of the conjunctiva. The International Organization Against Trachoma has as its founders Sédan, Nataf, Pagès, and Mawas. The prophylactic treatment of blennorrhea has immortalized the name of Crédé. Magitot arrived at the conclusion that glaucoma is essentially the result of a disturbance in the capillary permeability. Lagrange was the first to introduce sclerectomy in 1906 which has become the prototype of all filtering operations. Bailliart's research on retinal circulation has become a classic. This rather incomplete list will have to suffice as representative of some of the most important contributors to French ophthalmology cited by Onfray.

Giuseppe Ovio, in order to do justice to the importance of ophthalmology in Italy, has to trace its contributions from ancient Roman times to this day. The treatment of eye diseases, as in all other European countries, originally was not a specialty but was at first in the hands of barbers, later in the hands of general surgeons. It was in Italy that spectacles were invented toward the end of the 13th century. Not only anatomists like Bartolomeo Eustacchio and Gabriele Falloppio come to mind. The universal genius of Leonardo da Vinci has left his indelible imprint on that epoch. Antonio Benevoli was first to recognize cataract as a disease of the lens. He also diagnosed retinoblastoma in a baby. The names of Felice Fontana, Giovanni Battista Morgagni, and Antonio Maria Valsalva also should be mentioned here. From the second half of the last century the names of Carolo de Vincentiis (associated with goniotomy) and Camillo Golgi (for his histologic studies of the nervous system with his silver stain) are singled out.

A. Pillat comments on the history of ophthalmology in Austria by describing the history of the 1st and 2nd Augenklinik in Vienna. One certainly could not think of a more appropriate approach. In his inimitable manner he covers the period from 1773 when Joseph Barth became the first professor of ophthalmology by the grace of Empress Maria Theresia to this day of his directorship of the 1st Augenklinik as worthy successor of a proud line of men whose names are living history for at least the older generation of American ophthalmologists.

F. Rintelen concerns himself with Brückner's scientific importance in the framework of German ophthalmology between 1870 and 1920 (Brückner left the University of Jena in 1923 to accept the chair of ophthalmology in Basel). Brückner's interest in physiology was aroused by his contact with Ewald Hering. His clinical teachers were Carl v. Hess and Emil Krückmann. This should explain Brückner's dual interest in the field of physiology and optics, as well as in clinical ophthalmology. A very complete table lists the names of all the heads of the departments of ophthalmology and their terms of tenure at every German university, beginning with Chr. G. Th. Ruete, who became the first professor of ophthalmology in Göttingen in 1848, up to the present day.

W. P. C. Zeeman, reporting on the history of ophthalmology in the Netherlands, stresses mostly the contributions made by his compatriots in the basic sciences. Most of them were not physicians. As early as the second half of the 17th century Christiaan Huygens published his fundamental work in the field of optics. Einthoven prepared the way for Smit's and Henke's research on electroretinography. Donders' work has been epochal. E. P. Fischer's investigations of the

gaseous metabolism of the eye cannot be overemphasized.

This review covers only the highlights of this most stimulating brochure. Every ophthalmologist with even a smattering knowledge of German, French, and Italian (only Duke-Elder wrote his chapter in English) will spend a few most enjoyable and profitable hours perusing this stimulating and revealing pamphlet.

Stefan Van Wien.

VETERINARY OPHTHALMOLOGY. By R. H. Smythe, M.R.C.V.S. Second edition. Baltimore, Williams and Wilkins Co., 1958. 379 pages, 59 illustrations, index. Price: $8.50.

The second edition of this popular text comes only two years after the first publication. Here the modern knowledge of ophthalmology is adapted to the study and treatment of animals. The first 108 pages discuss the anatomy and physiology of the eyes of the dog, cat, rabbit, pig, sheep, horse, cow, and other animals. The rest of the volume is purely clinical. Bibliographic references are placed at the close of each of the 14 chapters. Though the work is designed primarily to be of practical value to the veterinary practitioner, it should be helpful to the research worker and to all others who are interested in animal life and behavior.

James E. Lebensohn.

CHEMISTRY AND BIOLOGY OF MUCOPOLYSACCHARIDES. G. E. W. Wolstenholme and M. O'Connor, editors. Ciba Foundation Symposia. Boston, Little, Brown and Company, 1958. 323 pages, 48 illustrations, author and subject indices. Price: $8.50.

Since the discovery of hyaluronic acid in the vitreous by K. Meyer in 1934, the group of compounds known as mucopolysaccharides (or mucoproteins when attached to a protein molecule) has been of great interest to ophthalmologists. In addition to their historic importance in the vitreous, polysaccharides have taken on new significance through the work of Dische on the lens capsule, Bárány on the trabecular meshwork, and Meyer on the cornea. However, with the elaboration of these compounds in various tissues, a goggle of polysyllabic names has arisen so that there is today no universally acceptable definition of the term mucopolysaccharides. In order to clarify this situation and perhaps to impose some order on this rapidly growing subfield of chemistry, a conference under the auspices of the Ciba Foundation was held in London in April, 1957. Ophthalmologists should take pride in the fact that our own Dr. Dische was instrumental in organizing this symposium and his paper entitled "Neutral heteropolysaccharides in connective tissue" reports his most recent finding on the mucoproteins of the vitreous. The remainder of the papers are rather technical and will be of interest primarily to investigators in the field of biochemistry of the eye.

David Shoch.

THE EVIL EYE. Studies in the folklore of vision. By Edward S. Gifford, Jr., M.D. New York, The Macmillan Company, 1958. 216 pages, bibliography, index. Illustrations by Virginia Mason Gifford. Price: $4.95.

This is an interesting discussion of the superstitions and folklore of the eye. If you think that this is all a part of the primitive past, you will be agreeably mistaken for it exists in modern society. Dr. Gifford of Philadelphia is assistant professor of ophthalmology, Graduate School of Medicine, University of Pennsylvania. Several articles on the *evil eye* by him have appeared in THE JOURNAL and our readers will recall them with pleasure.

The subject is an entertaining one to ophthalmologists. The text represents enormous reading in the classics of the ancient world,

as well as the various books on anthropology and so forth, to which a glance at the voluminous bibliography will testify. None of us has realized the danger of our jobs. "I saw a physician," wrote Roger Bacon, according to the author, "made blind while he was endeavoring to cure a patient with a disease of the eyes."

Strabismus, polycoria, nystagmus, and so forth are manifestations of the evil eye. A person possessing such an appendage can cause ocular diseases (cataracts, for example) just like that, as well as dry up cow's milk, separate lovers, cause chilblain, and about every woe to which we are heir. If the etiology is simple, the cure is easy. Urine, mother's milk, and spit are good therapeutic agents, or at least considered to be prophylactic ones. And apparently, while times have changed, the amount of our fees has remained the same and the risks of malpractice are greater.

Dr. Gifford writes well, with a nice sense of humor. You will enjoy the book very much indeed.

Derrick Vail.

GUIDE TO OCCUPATIONAL AND OTHER VISUAL NEEDS. Volume I. By C. Holmes, H. Jolliffe, J. Gregg, I. S. Cameron and R. Blyth. Distributed through Clark Holmes, P.O. Box 5310, Metro Sta., Los Angeles 55, 1958. 482 plus xiv pages profusely illustrated, index. Price: $12.50.

For years the optical companies have sought to increase their sales by promotional literature emphasizing from many aspects that one pair of glasses is not enough—that social, vocational, and avocational requirements demand at least separate glasses for dress and business, absorptive lenses for outdoor glare, and special prescriptions for work and play. This guide, in the format of *Life* with two or three illustrations on each large page, demonstrates in graphic detail that lenses for general use frequently cannot meet all the occupational requirements in presbyopic patients. The authors studied the working distances of pre-presbyopes, as otherwise the working position is influenced by the bifocals worn. Every occupation was carefully observed and photographed. Occupations such as pharmacist, grocer, and shoe-clerk have a working distance of 18 inches. An accountant needs clear vision at 16 inches for his immediate work, but must see at 26 inches the ledger to one side. A photoengraver requires a high bifocal with a relatively strong add. The housewife performs dish-washing at 20 inches, ironing at 24 inches. A secretary needs a range of 20 inches for filing, 24 inches for copying. The excellent index lists almost all occupations and hobbies from artist and archery to trap-shooting and watchmaker. The introductory and concluding pages contain much informative material, including various tables, a vocational test chart, and a clever graph for determining the P.D. for near and intermediate distances. Russell Stimson, in his discussion of lenses for aphakics, remarks that a cataract lens is not damaged by careful resurfacing.

The publication of this work, the most ambitious effort ever undertaken in its field, was underwritten by 85 firms of the Association of Independent Optical Wholesalers, and is sold on a nonprofit basis. Reference to this work will give a clearer picture of a patient's job requirements than can usually be obtained from the patient himself.

James E. Lebensohn.

ABSTRACT DEPARTMENT

EDITED BY DR. F. HERBERT HAESSLER

Abstracts are classified under the divisions listed below. It must be remembered that any given paper may belong to several divisions of ophthalmology, although here it is mentioned only in one. Not all of the headings will necessarily be found in any one issue of the Journal.

CLASSIFICATION

1. Anatomy, embryology, and comparative ophthalmology
2. General pathology, bacteriology, immunology
3. Vegetative physiology, biochemistry, pharmacology, toxicology
4. Physiologic optics, refraction, color vision
5. Diagnosis and therapy
6. Ocular motility
7. Conjunctiva, cornea, sclera
8. Uvea, sympathetic disease, aqueous
9. Glaucoma and ocular tension
10. Crystalline lens
11. Retina and vitreous
12. Optic nerve and chiasm
13. Neuro-ophthalmology
14. Eyeball, orbit, sinuses
15. Eyelids, lacrimal apparatus
16. Tumors
17. Injuries
18. Systemic disease and parasites
19. Congenital deformities, heredity
20. Hygiene, sociology, education, and history

1

ANATOMY, EMBRYOLOGY, AND COMPARATIVE OPHTHALMOLOGY

Busse Grawitz, P. **Reply to Heydenreich's paper on the leukocytes in the cornea.** Klin. Monatsbl. f. Augenh. **132**: 548-558, 1958.

This is a reply to a paper which appeared in an earlier issue (Klin. Mbl. f. Augenh. 130:512, 1957). In this paper Heydenreich had proved the derivation of the corneal leukocytes from the blood stream in experiments on animals made leukopenic by the administration of a nitrogen-mustard derivative. Busse Grawitz repeated and elaborated these experiments. He also found in such animals a suppression of the leukocytic reaction in a central corneal lesion, but the limbal leukocyte accumulation persists. He still is of the opinion that the corneal leukocytes are produced in the stroma and not transported by the bloodstream. (2 figures, 11 tables, 20 references)

Frederick C. Blodi.

Carreras, Marcelo. **The sparing of the macula in congruent homonymous hemianopsia. The imbrication of heteronymous hemianopic visual fields and the significances of Gudden's commissure in man.** Arch. Soc. oftal. hispano-am. **18**:191-200, March, 1958.

The recent literature relevant to the elucidation of the mechanism of sparing of the macula in homonymous hemianopsia is reviewed. By correlating the data gathered from the literature the author concludes that Gudden's commissure is the anatomic area concerned in macular sparing or loss. The author believes that the macular fibers and the fibers corresponding to the region about the vertical meridian of the visual field divide behind the chiasm; the direct homolateral fibers are joined by the crossed fibers from the opposite eye and proceed to the external geniculate body. Two visual neurons leave the external geniculate body, one in the optic radiation toward the occipital cortex. The other neuron proceeds through Gudden's commissure and reaches the external geniculate body of the opposite side and through the optic radiation reaches the occipital cortex of the opposite side. Retrochiasmal lesions which affect Gudden's commissure produce a homonymous hemianopsia with bisection of the macula. The hemianopsia associated with retrochiasmal lesions which do

not involve Gudden's commissure spares the maculas. Wolff's recent investigations showed that Gudden's commissure is connected not with the internal but with the external geniculate body, and its function is visual and not acoustic. Long ago Cahal demonstrated the presence of optic fibers in Gudden's commissure by producing degenerative changes in the commissure in new-born cats after section of both optic nerves. The clinical findings are understood if it is agreed that the visual fibers run in Gudden's commissure. It is possible that another mechanism exists which saves the macula in lesions of the posterior portion of the optic pathway. (6 figures, 10 references) Ray K. Daily.

Hueck, H. and Kleifeld, O. **An electron-microscopic study of the lens fiber.** Arch. f. Ophth. **160**:20-25, 1958.

Sections of guinea pig lenses embedded and stained by various methods were studied with the electron-microscope. It seems possible that each fiber has its own membranous sheath and that there is a minute intercellular space between fibers. Very small oval structures were also seen within the fiber. (7 figures, 9 references) F. H. Haessler.

Nordenson, J. W. **New arguments in the question of the color of the macula.** Arch. f. Ophth. **160**:43-46, 1958.

The author discusses Brueckner's argument for the existence of yellow coloring in the macula and finds it unconvincing. Other evidence is contributed by two English biochemists, Keilin and Smith, who noted two diffuse absorption bands which are visible with a pocket spectroscope or a microscope with microspectroscopic ocular. These absorption bands are seen in what has been considered a continuous subjective spectrum. The author has been unable to confirm the findings. Apparently the question is again an open one. (10 references) F. H. Haessler.

Wolter, J. Reimer. **Reactions of the cellular elements of the corneal stroma.** A.M.A. Arch. Ophth. **59**:873-881, June, 1958.

The author reports the histologic changes in the rabbit's cornea following experimental trauma and especially compares the stromal cells with the cells which invade the stroma secondarily. The corneal stroma cells are distinctly different from the invading fibroblasts, even in their reactive and migrating forms. The lymphocytes and leukocytes were found to immigrate from the limbus. (16 figures, 8 references) G. S. Tyner.

2

GENERAL PATHOLOGY, BACTERIOLOGY, IMMUNOLOGY

Collier, L. H. and Sowa, J. **Isolation of trachoma virus in embryonate eggs.** Lancet **1**:993-996, May 10, 1958.

The trachoma virus was isolated from the conjunctival scrapings of a Mandingo girl. The virus was given ten yolk sac passages, morphologic study, staining reactions, electron microscopy, and serologic tests. The conjunctiva of a man who had both eyes removed for phako-anaphylactic endophthalmitis was inoculated with the virus. Typical lesions seen in early trachoma developed and initial body forms and Halberstaedter-Prowazek bodies were found in the conjunctival scrapings. Material taken from the subject's eyes were inoculated into chick embryos where the characteristic bodies and hemorrhagic lesions were shown in yolk sac smears. (3 figures, 1 table, 13 references) Irwin E. Gaynon.

Keckarovski, A. **A contribution to the experimental study of the allergic processes of the anterior segment of the eye.** Brit. J. Ophth. **42**:288-295, May, 1958.

Various antigens, mostly human, horse, pig and ox sera, were injected into parts

of the anterior segments of rabbit eyes and the local anaphylactic processes were studied. At the site of the injection there was usually an immediate reaction which disappeared in several hours. Some eyes were sensitized in one and some in both eyes and some received a second injection of the same or of a different antigen.

A general pattern of reaction was noted. A primary early reaction, if severe, was always followed by a late reaction. If both eyes were sensitized the late reaction was binocular; this occurred even if a different antigen was used in each eye. The author assumes that in addition to a humoral element causing these reactions, there must be also a neuroreflex factor. (4 figures, 3 tables, 23 references)

Morris Kaplan.

Österlind, Göte. **Experimental studied on the elective sensitization of the uvea.** Acta ophth. **36**:244-272, 1958.

If one eye of an experimental animal is exposed to a strong antigen intense sensitization of the uvea of both eyes sometimes occurs. In such cases the subsequent systemic introduction of the specific antigen will elicit an allergic uveitis in both eyes of the experimental animal. This phenomenon, which has been called elective sensitization of the uvea, was investigated. Development of an elective sensitization required that the allergic uveitis in the eye treated with antigen was of medium intensity and duration. If uveitis in that eye assumed the character of a panophthalmitis with complete destruction of the uvea, no elective sensitization occurred. Elective sensitization of the uvea develops some time after generalised horse serum allergy has been established. If the eye treated with antigen is enucleated during the latent period, a generalized horse serum allergy will develop but no elective uveal sensitization. It seems probable that the uvea plays an active role in the development of elective sensitization, but no convincing evidence that it does so by participating in the formation of an antigen which leads to a release of specific uveotoxic antibodies was found. (5 figures, 6 tables, 33 references) John J. Stern.

3

VEGETATIVE PHYSIOLOGY, BIOCHEMISTRY, PHARMACOLOGY, TOXICOLOGY

Auricchio, G. and Wistrand, P. **Chloride content of the aqueous during experimental uveitis.** Acta ophth. **36**:304-308, 1958.

In unilateral anaphylactic uveitis of the rabbit the chloride level in the aqueous in the inflamed eye falls below that of the healthy eye. (1 table, 15 references) John J. Stern.

Cristiansson, John. **Changes in mucopolysaccharides during alloxan diabetes in the rabbit. I. Comparative studies on serum and the hyaluronic acid of the vitreous body.** Acta ophth. **36**:141-162, 1958.

Two to four weeks after the administration of alloxan a significant increase in the protein-bound carbohydrates of the serum appears which is progressive and unaffected by insulin. The hyaluronic acid of the vitreous is subject to changes parallel to those in the serum. The volume of the vitreous body gel is reduced as the viscosity and the hyaluronic acid content increase. (8 figures, 5 tables, 42 references) John J. Stern.

Cristiansson, John. **Changes in the mucopolysaccharides during alloxan diabetes in the rabbit. II. Studies of intraocular pressure.** Acta ophth. **35**:163-177, 1958.

Tonometry and tonography were done over a period of three or four months in rabbits with alloxan diabetes. When insulin was withheld from the animals, there was an average reduction of the ocular tension of 6 mm. Hg. Simultaneous deter-

minations of bicarbonate in the blood plasma showed reduced values, corresponding to a more or less pronounced acidosis. Insulin restored the intraocular pressure to normal levels, while the coefficient of facility of outflow decreased considerably. This has been taken as evidence of an increased anatomic barrier in the form of a mucopolysaccharide, obstructing the outflow of the aqueous humor. (6 figures, 4 tables, 34 references)

John J. Stern.

Cristiansson, John. **Transient myopia after the administration of diamox.** Acta ophth. **36**:356-357, 1958.

Transient myopia occurred in a pregnant woman 27 years old who was given three tablets of diamox for edema of her legs and hands. Mild signs of iritis and subnormal ocular tension were also observed. A diamox-induced acidosis is considered a possible cause for the symptoms which lasted less than two days. (3 references) John J. Stern.

De Conciliis, Ugo. **Rhodanese and Rhodanese S activity in ocular fluids.** Arch. di ottal. **61**:455-460, Nov.-Dec., 1957.

Potassium thiocyanate is a constituent of normal body tissues and is detoxified by transulfurase of Rhodanese enzymes. Previous reports had stated that tissues with elevated glycolysis such as the retina and neoplastic tissue have low transulfurase activity. Experiments with beef and rabbit aqueous and vitreous showed low Rhodanese S activity by the method of Ruffo-Romano and Giampaolo. (1 table, 10 references) Paul W. Miles.

De Conciliis, Ugo. **Histologic and metabolic changes in the eyes in rats deprived of zinc.** Arch. di ottal. **61**:505-513, Nov.-Dec., 1957.

Recent studies of the physiologic action of zinc have shown certain enzyme reactions essential to health. Lack of traces of zinc in the diet retards growth, diminishes or depigments hair, changes the curve in glucose tolerance tests, causes hypoproteinemia, decreases amylase and pancreatic protease, decreases intestinal phosphatase, reduces excretion of uric acid, and causes hyperkeratinization. In 20 rats deprived of zinc, it required 65 days to show superficial vascularization of the cornea, infiltration of the stroma with polymorphonuclear leukocytes, and vacuolization of the basement membrane of corneal epithelium. These changes resembled those of riboflavin deficiency. (2 figures, 2 tables, 7 references)

Paul W. Miles.

De Rosa, L. **Phosphatase in the cornea and lens.** Arch. di ottal. **61**:475-486, Nov.-Dec., 1957.

Enzymes releasing ionic orthophosphoric acid have been shown in many animal and vegetable tissues. By a new histochemical technique, phosphatase activity was measured in beef corneal epithelium and endothelium and lens epithelium under various conditions of pH, temperature, time, and buffering. Phosphatase was found to be nearly zero in the corneal stroma, very little in the endothelium compared to that in the epithelium of the cornea and lens. The phosphatase activity was increased by $MgCl_2$ and was decreased by NaF at various concentrations. The phosphatase activity was greater in the cornea than lens epithelium, and responded to the $MgCl_2$ and NaF in a parallel manner. Optimum glycerophospholysis exists at pH 9.31 and at pH 4.66 in both lens and cornea. (4 figures, 5 tables, 29 references) Paul W. Miles.

Dyster-Aas, K. and Krakau, C. E. T. **A microrheometer for perfusion of the eyes.** Acta ophth. **36**:178-182, 1958.

The instrument is described in detail. (4 figures, 4 references)

John J. Stern.

Furuse, A. **Mode of action of diamox on ocular tension.** Acta Soc. Ophth. Japan **62**:274-277, 359-363, 480-485, 571-578, March, April, May, -958.

A subconjunctival administration of diamox usually has no effect on ocular tension in rabbits. It sometimes causes an increase in ocular tension with a definite local irritation. By systemic administrations, a lowering of ocular tension results with a lowering of systemic blood pressure. A delay in the aqueous outflow is demonstrated after diamox administration by tonometry. The entrance of fluorescein, intravenously administered, into the aqueous is made sluggish by diamox, the highest concentration of the dye in the aqueous becomes low, and the disappearance of it from the aqueous delayed. Furase concludes that the lowering of the tension by diamox is not due to an acceleration of aqueous outflow. (9 figures, 6 tables, 102 references)

Yukihiko Mitsui.

Graymore, Clive. **Swelling of the rat retina induced by metabolic inhibition.** Brit. J. Ophth. **42**:348-354, June, 1958.

Preliminary work is reported which indicates that metabolic inhibition of cells by iodoacetate and fluorides may be a cause of retinal edema because of its vaso-obliterative effect. (3 figures, 1 table, 17 references)

Lawrence L. Garner.

Hockwin, O. and Bergeder, H. D. **The effect of Röntgen irradiation in large dosage on the oxygen absorption of the lens.** Arch. f. Ophth. **160**:1-7, 1958.

The authors discuss known biochemical results of exposure to ionizing rays. They report their own measurements of the absorption of oxygen by the lens of the guinea pig before and after irradiation with 90 kr. In vitro experiments showed that the absorption of oxygen after irradiation is greatly increased in lenses of the embryo, is diminished in young lenses and remains unchanged in lenses of the old animal. (5 figures, 33 references)

F. H. Haessler.

Hockwin, O., Neumann, H. G. and Kleifeld, O. **The lens proteins in relation to age in the lenses of guinea pigs and cattle.** Arch. f. Ophth. **160**:8-19, 1958.

The authors find that the synthesis of protein and, as a result, the composition of crystallin is not the same in the embryonal fiber as in the postembryonal. Moreover, it seems probable that the crystallin synthesis in the postembryonal lens fibers is dependent upon the time of its origin. First there is an increase of the total crystallin in which all three crystallin fractions increase proportionately, then a reduction of total crystallin, particularly of fraction I and a marked increase of water-soluble protein. In the aged animal there is a great increase of fraction III in the nucleus of the lens but it seems questionable that this fraction III is composed of the same proteins as in the young lens. (6 figures, 8 tables, 13 references)

F. H. Haessler.

Huggert, A. and Esklund, A. **The location of the chief obstruction to the outflow of the aqueous humor from the eye of cattle.** Acta ophth. **36**:50-56, 1958.

Dyes and suspensions of stained particles were injected into the anterior chamber or the aqueous veins of the eyes of cattle. Most of the particles were checked at the vessels corresponding to the canal of Schlemm, and the vascular wall constituted the chief obstruction. In some cases the stained particles formed rows that were disposed radially around these vessels; this suggests blocking of canals or tubules in the inner part of the filtration angle that are connected with the Schlemm system. (4 figures, 8 references)

John J. Stern.

Kobayashi, M. **Studies of the lacrimal gland by electron microscopy.** Acta Soc. Ophth. Japan **62**:230-241, Feb., 1958.

The lacrimal gland of rabbits was studied in sections by electron microscopy. The changes induced by pilocarpine administration were followed. The gland cells are morphologically divided into four forms according to the stage of secretion. (12 figures, 20 references)

Yukihiko Mitsui.

Krakau, C. E. T. **The potential field of the rabbit electroretinogram.** Acta ophth. **36**:183-207, 1958.

The potential field of the ERG has been studied in a volume conductor in front of the eye, inside the eye, and in the retrobulbar tissue. The internal potential is almost constant in air and the same as the corneal potential. The retrobulbar potential is low. The moment of the posterior part of the retina is given by the corneal potential.

In a volume conductor the potential increases from outside along an S-shaped curve through the eye when the electrode is introduced axially. The maximum point is in front of the retina. The retrobulbar potential is increased and opposite in sign to the corneal potential. The moment over the retina is probably somewhat reduced by the introduction of a volume conductor.

The character of the field is consistent with the hypothesis that a double layer is present in the wall of the eye. The moment of this layer increases from the limbal region to the posterior pole, as judged from the surface potential in air. Changes in the internal *emf* can be brought about by alterations in the direction of stimulating light. They are observable on the surface of the bulb in air, most clearly over the posterior parts. In a volume conductor the changes in the field can also be recorded in the anterior regions. (13 figures, 1 table, 10 references)

John J. Stern.

Küchle, H. J. and Rohrschneider, W. **Electroshock and intraocular pressure. III. Report.** Arch. f. Ophth. **160**:98-112, 1958.

The authors made 60 experiments with rabbits to determine whether changes in ocular tension which followed electroshock could be ascribed to the effect of the shock on the vegetative nervous system. The condition of the pupils indicated a considerable stimulation of the parasympathetic system. The suggestion that the decrease in tension was the result of an increased formation of acetylcholine was not adequately clarified by the injection of the substance. However, the injection of atropine, to reduce the sensitivity of the parasympathetic, before exposure to electroshock, suggests that the parasympathetic sensitivity which is brought about by the electroshock is an important tension-reducing factor. (6 figures, 2 tables, 24 references)

F. H. Haessler.

Laffers, Z. and Bozsóky, S. **Clinical significance of determination of antistreptolysin in the aqueous humor.** Szemeszet **2**:49-56, 1958.

Normal aqueous humor contains no antistreptolysin but in uveitis antistreptolysin appears irrespective of the pathogenesis of the inflammation. On the basis of the observations, an intraocular antistreptolysin production seems to be possible and is suitable to prove the diagnosis of streptogenic uveitis. A fluctation of the antistreptolysin level indicates a streptogenic uveitis. Gyula Lugossy.

Levene, Ralph Z. **Sodium and potassium concentrations following acetazolamide.** A.M.A. Arch. Ophth. **59**:868-872, June, 1958.

Acetazolamide produces a decrease in

the potassium concentration of aqueous and plasma for at least five hours after administration of the drug. No alteration of the sodium concentrations of the two fluids is obtained two and one-half hours after the drug is given. (7 tables, 32 references) G. S. Tyner.

Majima, Y. **Change of adenosine triphosphatase and 5-nucleotidase in visual cells by light and dark adaptation.** Acta Soc. Ophth. Japan 62:185-190. Feb., 1958.

The activity of the enzymes was measured by various methods in bovine, rabbit, and frog retinas. The activity of adenosine triphosphatase in visual cells is increased by dark adaptation, and in other parts of the retina the converse is true. The activity of 5-nucleotidase in the retina is increased 50 percent by light adaptation. (2 figures, 2 tables, 22 references) Yukihiko Mitsui.

Nilausen, Karin. **The vasoformative tissue in the fetal retina with particular reference to the histochemical demonstration of its alkaline phosphatase activity.** Acta ophth. 36:65-70 1958.

The presence of alkaline phosphate activity in the human fetal retina was demonstrated histochemically. The material consisted of human fetuses weighing 200 to 600 grams. The entire vascularized area is phosphatase positive; the surrounding avascular zone is phosphatase negative. The enzyme, like the vascular system in this weight group, is found only in the nerve-fiber layer. Retinas still unvascularized show no enzyme activity. The phosphatase activity is associated with 1. the cell formation at the periphery of the advancing vascular system, 2. the endothelium of the peripheral capillaries, and 3. the cells scattered between the vessels. (4 figures, 6 references) John J. Stern.

Orzalesi, F. and Miglior, M. **Concerning the interactions between lens proteins and other proteins. Preliminary note on the possibility of fractional precipitation of lens proteins by means of electropositive proteins.** Arch. d'opht. 17:782-790, Dec., 1957.

The authors refer to their previous studies in which they showed that electropositive proteins added to aqueous extracts of lens substance could react, at physiologic pH levels, with certain soluble lens proteins and lead to the formation of insoluble complexes. They also showed that when basic proteins were inoculated into the vitreous, a similar precipitation effect could be obtained in vivo in the rabbit as a result of passage of these proteins through the normal lens capsule. A cataract was produced, commencing in the posterior subcapsular layers, which resembled greatly the complicated cataract seen in humans.

In the present study the authors report the modifications of the protein composition of normal rabbit lenses that are induced by mixture with electropositive proteins. The precipitate obtained is sedimented by rapid centrifugation and the supernatant liquid was used for electrophoretic analysis. The significance of these analyses is considered and the possible relationship of these phenomena to the mechanism of cataract is discussed. P. Thygeson.

Pivont, A. and Gongnard, L. **A new mydriatic, the 2-2 diphenyl-4 hexamethyleneamino-butyramide hydrochloride (R 658).** Bull. Soc. belge d'opht. 177:506-510, 1958.

R 658 is a specific parasympatholytic agent. Its mydriatic and cycloplegic effect was studied in 45 normal eyes and the results were compared with the action of atropine. A 1-percent aqueus solution was used. Its mydriatic effect ressembles that of atropine but is more prolonged. Its cycloplegic action is less pronounced. It also has a mild anesthetic action. The

ensuing pupillary changes and the relaxation are summarized on two charts. R 658 is a product of Eupharma de Turnhaut. (2 figures, 2 references)

Alice R. Deutsch.

Sakaue, E. **Influence of thyroid hormone on the distribution of vitamin B_1 in ocular tissues.** Acta Soc. Ophth. Japan **62**:48-53, 121-124, Jan., Feb., 1958.

When thyrotropic hormone of the anterior pituitary, Pretiron (Schering), is administered into rabbits with vitamin B_1, a greater increase in cocarboxylase occurs in blood and ocular tissues than by an administration of the vitamin alone. This may be due to an acceleration of esterification by the hormone. The hormone alone has no effect. Methiocil (4-methyl-2-thiouracil), when administered into rabbits every day for two weeks causes an increase in thiamin and cocarboxylase of the ocular tissues, particularly those of the retina. It also causes a hyperemia and enlargement of the thyroid gland. (2 figures, 2 tables, 15 references)

Yukihiko Mitsui.

Szeghy, G. **Local effect of heparin on experimental lesions of the cornea.** Szemeszet **2**:57-62, 1958.

Experimental corneal lesions are favorably influenced by heparin ointment and solution. Hyperemia and edema of the conjunctiva diminish or cease. Vascularization of the cornea may be inhibited by heparin. Epithelial regeneration is enhanced. As seen from comparison with the controls, scars and opacities also are favorably influenced. Its antiphlogistic effect is inferior to that of cortisone, while the inhibition of corneal vascularization, the promoting effect on epithelial regeneration, and the inhibition of opacity formation, are much the same as the corresponding cortisone effects. In certain cases heparine may be used as a substitute for cortisone. No side effect was observed. Drops and ointment are equally useful. The mechanism of its action is unknown. Gyula Lugossy.

Vörösmarthy, D. and Benko, K. **The physical and biological bases of solar coagulation.** Szemeszet **95**:1-5, 1958.

The authors examined whether direct sunlight is suitable to perform bloodless intraocular interventions. On the basis of local meteorologic factors the authors tried to establish by calculations the intensity and the quantity of sunshine arriving on the earth's surface. Warming has been measured directly by means of a thermistor placed on the choroid of a rabbit's eye. It has been found that direct sunshine is sufficient to raise the temperature of the choroid to the degree necessary to coagulate the proteins, that is, to produce irreversible changes in the eye. Gyula Lugossy.

Waki, M. **Effect of diamox on potassium concentration in blood and aqueous.** Acta Soc. Ophth. Japan **62**:267-275, 487-492, March, May, 1958.

When diamox is given to rabbits intravenously in a dosage of 30 mg. Kg. body weight, the potassium in serum and aqueous decreases by 9 percent and 22 percent, respectively, in two hours. The effect lasts for six hours showing a w-shaped variation curve. The increase in the potassium of aqueous and serum after an intravenous administration of potassium chloride is impeded when diamox is given previously. The potassium increase in the serum becomes about one half of that of the diamox-free control animals which were not given diamox. In animals with injected diamox the potassium in the aqueous continues to decrease even after an administration of potassium chloride. This effect of diamox lasts for 150 minutes. (4 figures, 7 tables, 63 references)

Yukihiko Mitsui.

Wistrand, Per. **The failure of promethazine and chlorpromazine to prevent the pressure response of the eye to local irritation of the iris.** Acta ophth. **36**:26-32, 1958.

Promethazine was introduced into the aqueous of rabbits and injected subcutaneously in doses of 25 to 100 mg. per kg. body weight, and chlorpromazine was administered subcutaneously in a dose of 5 mg. per kg. body weight. Neither drug blocked the response to local irritation of the iris made manifest as a change in eye pressure. The experiments raise the question whether histamine is responsible for the pressure response by change in pressure and the vascular reaction following injury to the iris or cornea. (4 figures, 18 references) John J. Stern.

Yamada, H. **Phase contrast microscopy of the vitreous.** Acta Soc. Ophth. Japan **62**:162-175, 497-508, Feb., May, 1958.

This is an observation of the vitreous in the young dog by phase microscopy after an injection of blood or trypsin into the vitreous. The blood can be absorbed in three months. Phagocytes appear in the vitreous to take the blood cells in. After the absorption of the blood, a degeneration of vitreous fibers remains. The iron reaction is positive in the vitreous for four months. An intravitreous injection of trypsin of high dosage causes a severe inflammation in 24 hours and also a degeneration of vitreous fibers. With a low dosage of trypsin the vitreous membrane is affected and tear formation occurs. (45 figures, 23 references)

Yukihiko Mitsui.

Yoshizawa, T. **Biochemical studies of the secondary aqueous humor.** Acta Soc. Ophth. Japan **62**:202-218, 442-453, Feb., April, 1958.

The author reports a chronologic examination of the second aqueous in rabbits. For the first 30 minutes after a puncture the albumin fraction increases and then α-globulin increases. After 10 hours the albumin-globulin ratio reaches a minimum. It takes 24 hours until the aqueous regains its original constitution. The change in the sodium and potassium ion, amino acids and residual nitrogen of the aqueous is also discussed. The concentration of sodium ion in the aqueous is essentially constant throughout the course and is the same as that in serum. The potassium concentration is higher in the primary aqueous than in serum. In the early secondary aqueous there is a temporary rise in potassium concentration which is followed by a rapid decrease. Yoshizawa consider that the sodium ion passes freely through the blood-aqueous barrier but the potassium ion does not. (34 figures, 13 tables, 35 references) Yukihiko Mitsui.

4

PHYSIOLOGIC OPTICS, REFRACTION, COLOR VISION

Belcher, S. J., Greenshields, K. W. and Wright, W. D. **Color vision survey.** Brit. J. Ophth. **42**:355-359, June, 1958.

After using 500 subjects in a color vision survey and five different sets of confusion charts, the authors conclude that errors are noted in any of the present methods of testing. A good screening test should divide the color blind from the normal (two distinct groups) but this study presents a definite overlap of borderline cases irrespective of the test used. The Nagel anomaloscope is suggested as a means of identifying the occasional borderline case. A factor in maintaining integrity of the confusion charts is the ability of the printer to keep his color quality intact. (2 tables, 6 references) Lawrence L. Garner.

Brolin, S. E., and Cederlund, C. **The fluorescence of the lens of different species.** Acta ophth. **36**:324-328, 1958.

Considerable differences in the intensity of fluorescence were found in different species. The highest intensity was found in guinea pigs and frogs, the lowest in haddocks and rats. (2 figures, 4 references) John J. Stern.

De Laet, H., Szucs, S. and Leblois, I. **The treatment of extra-foveal fixation and of amblyopia with Cupper's method of after-images.** Bull. Soc. belge d'opht. 117:468-482, 1957.

In the method which has been previously described, a central area of the retina 30° in diameter is illuminated with a special ophthalmoscope, the euthoscope oculus. In the center of this bright pencil of light a small screen, 5° by 3° had been interposed. The area of this screen is focused exactly on the retina for a period of 20 seconds. The resulting after-image viewed over a clear surface layer causes an inhibition of the para-foveolar region while the protected fovea regains at least for some seconds its normal dominance. By repetition this dominance should be enforced until central fixation finally has been achieved. The course of treatment in 92 patients is described. The results were not favorable, with 20 percent failures, especially among patients 15-years-old and older. The basic conception of the treatment is attractive and the fundamental principles are certainly acceptable. The technique itself however is extremely difficult and improvement really could be expected only under especially favorable conditions. (4 tables) Alice R. Deutsch.

Elenius, V. and Zewi, M. **Flicker electroretinography in six cases of total color blindness.** Acta ophth 36:19-25, 1958.

Six totally color-blind persons were examined. In four cases a scotopic type of flicker ERG was found and the maximal FFF varied between 12 and 22 per sec. The flicker response was absent in one case when the illuminance was raised to 40 lux, and in the other three cases to 100 lux. In two cases scotopic and photopic flicker potentials could be recorded. The maximal FFF reached normal values only when the stimulus intensity was higher than in normal eyes. Apparently in these two "atypical" cases of total color blindness a part of the total number of cones was functional (3 figures, 9 references) John J. Stern.

François, J. and Verriest, G. **A particular kind of essential hemeralopy.** Bull. Soc. belge d'opht. 117:630-641, 1957.

The pathologic entity under discussion is characterised by a slow dark adaptation with elevation of both segments of the adaptation curve and late gradual normalization and by an electro-retinogram with a normal b_1 wave with retardation of the b_2 part.

The patient, a 42-year-old woman, had been conscious of her handicap all her life. She had a hepatitis when she was 20 years old and even 22 years later the cholesterol-ester and gamma-globulin levels were not completely normal. The vitamin A and carotenoid levels were within normal limits. The eye findings were normal except for a mild disturbance in the perception of green. The EEG was normal. The hemeralopy could not be ascribed to a nutritional deficiency nor to a tapeto-retinal degeneration. It also did not resemble an essential hemeralopia, characterised by a monophasic adaptation curve. Adaptation changes similar to the ones described have been seen in Oguchi's disease but the patient did not show any color changes in the fundus. This congenital anomaly does not resemble any known form of hemeralopia. (8 figures, 6 references) Alice R. Deutsch.

Grüsser, O.-J. and Grützner, A. **The neurophysiologic basis for periodic after-image phases after brief light flashes.** Arch. f. Ophth. 160:65-93, 1958.

Modern microelectrode methods make

it possible to register action potentials of individual nerve and receptor cells of the visual cortex. By this means one can analyze changes of activity in peripheral and central optic systems of experimental animals and compare them with subjective manifestations in man. The authors report studies in which they compare the reaction of individual retinal receptors, retinal nerve cells, and nerve cells of the primary optic cortex (area 17) of the cat after flashes, with subjective after-image phases after brief stimulation by light. They show that there is correspondence as regards time between subjective after-image manifestations and objective manifestation of stimulation. The variations in the cortical pattern of excitation which follow the very elementary pattern of stimulus of the light flash are determined predominantly by the pattern of retinal excitation. (7 figures, 3 tables, 90 references) F. H. Haessler.

Hoorens and Van de Velda. **Concave lenses should be placed close to the vertex of the cornea.** Bull. Soc. belge d'opht. 117:597-608, 1957.

It is disappointing to the highly myopic patient to find his vision with his new glasses inferior to the vision he had during the examination with lenses in the trial frame. The reasons for this distress is explained. With the modern concave-convex meniscus furnished by the optician the vision seems to be more strained as compared with the comfort with the old-fashioned biconcave or planoconcave lenses. Whenever a concave lens is placed farther away from the eye a stronger lens must be given. The retinal image also becomes smaller. Alice R. Deutsch.

Le Grand, Yves. **The protection of the eyes against ultraviolet light.** Ann. d'ocul. 191: 193-208, March, 1958.

The author divides the ultraviolet spectrum into three ranges: A—400 to 315 mμ, B—315 to 28 mμ, and C—280 to 180 mμ. Of these three only the first is ordinarily present in sunlight; the remaining groups are found primarily in the discharge of mercury lamps. Ordinary sunlight is harmless to the human eye unless the intensity is multiplied by water, snow, or sand. In the latter case glasses which absorb most of the ultraviolet B are necessary. Artificial fluorescent light is harmless. Sources of high intensity, ranges B and C, as found in industry should be guarded against. Naturally occurring ultraviolet, range A, is largely absorbed by the lens and thus does not effect the retina. However in aphakic eyes this normal absorbent of ultraviolet A is absent and some protection is advisable. (9 tables, 30 references) David Choch.

Linksz, Arthur. **Optics and visual physiology.** A.M.A. Arch. Ophth. 59:901-969, June, 1958.

This 60-page review is valuable not only because of its completeness, but also because of the apt comments of a learned author. (300 references) G. S. Tyner.

Mahneke, Axel. **Foveal discrimination measured with two successive light flashes.** Acta ophth. 36:3-11, 1958.

By systematically varying the duration of the dark interval between two successive light flashes, the author determined the relation between the quantity of light of the two flashes and the duration of the dark interval which just permits discrimination and fusion, respectively. If the ratio between the flash durations is 1, the dark interval decreases in an approximately rectilinear fashion, with the logarithm of increasing flash duration. If the ratio between the flash durations differs from 1, the dark interval also decreases with increasing quantity of light of the two flashes. The relationship mentioned does not hold when the flash 1 is of the duration 10 to 40 msec. and flash 2 is 1 to

3(4) msec. (3 figures, 1 tables, 20 references) John J. Stern.

Mahneke, Axel. **Fusion thresholds of the human eye as measured with two or several light flashes.** Acta ophth. **36**:12-18, 1958.

Determination of the dark intervals necessary for discrimination or fusion of two or more successive light flashes of constant luminance showed that for 17 different numbers of flashes (2 to 99) and six different flash durations (1 to 50 msec) the necessary dark interval may be shortened by 90 percent of the maximum reduction by increasing the number of successive light flashes from 2 to 11. At short flash durations (1 msec.) the dark interval reaches a constant value at 11-13 flashes. At long flash durations (50 msec.) this interval is not attained until the number of flashes has reached 39-49. At a given number of flashes the necessary dark interval may decrease when the flash duration is increased. During a given total duration of the intermittent stimulus, at a given luminance of the flashes, the largest number of cycles occur when the light: dark ratio is near 1. (2 figures, 9 references) John J. Stern.

Mayweg, S. and Massie, H. H. **Amblyopia ex anopsia.** Brit. J. Ophth. **42**:257-269, May, 1958.

For many years occlusion of the non-affected eye was the treatment of choice in amblyopia ex anopsia. Chavasse noted that some of these eyes did not respond to occlusion with improved vision because of eccentric fixation. In 1940 these patients were treated by "pleoptic treatment" which is an attempt to improve vision by exercises of coordination of hand, eye and brain. This form of therapy is now used frequently and several instruments have been evolved for restoring foveal fixation. The visuscope is a modified ophthalmoscope to diagnose eccentric fixation and the euthyscope and coordinator are used to restore central fixation.

With these instruments, 50 children aged four to 13 years were treated both as in-patients and out-patients. The number of treatments varied from five to 53 and results were generally quite satisfactory. In 38 cases the vision in the amblyopic eye was improved to 6/12 or better. It is urged that this after-image method of treatment be used more generally. (1 figure, 2 tables, 13 references) Morris Kaplan.

Schubert, G. **The neurophysiology of simultaneous contrast.** Arch. f. Ophth. **160**:94-97, 1958.

The author discusses the validity of current beliefs as to the interrelation between concepts of details of the neurophysiologic processes in the retina and of optic sensation. (13 references) F. H. Haessler.

5

DIAGNOSIS AND THERAPY

Bettman, Jerome W. **Radioactive isotopes.** A.M.A. Arch. Ophth. **59**:821-830, June, 1958.

This excellent article gives the author's technique and opinions on the use of radioactive isotopes in diagnosis, therapy, and experimental work in ophthalmology. The disadvantages are outlined and it is interesting that the author no longer uses it in attempting to diagnose retinoblastoma. He says that P^{32} tests have been very misleading and that pediatricians do not approve of giving small children P^{32} when their bone marrow is developing. (5 figures, 53 references) G. S. Tyner.

Bingen, F. **Postsurgical epithelial invasion into the anterior chamber.** Bull. Soc. belge d'opht. **117**:614-619, 1957.

The clinical appearance and development of epithelial invasion of the anterior chamber are discussed and a case history

is presented. The patient was seen two years after an uneventful extraction of cataract. Gonioscopic and slitlamp examination showed an advanced stage of the disease. A vertical incision into the membrane on the iris improved the visual acuity for six months; at this time an effort was made to excise the membrane from the iris. Nevertheless the retrocorneal membrane continued to grow and the eye remained periodically inflamed. The ocular tension, however, was never elevated. In reviewing the types of treatment employed the author discusses irradiation with X-ray in high doses, a treatment which mostly was not beneficial, removal of the invading epithelium with specially constructed curettes as recommended by Bangerter, another surgical method which was published by Long and Tynert. The latter curetted the epithelium with a chalazion curette and cauterize the denuded surface with 70 percent alcohol. Only one case out of three was successful. (4 references) Alice R. Deutsch.

Ferreira, Alberto Alfonso. **Ocular anesthesia.** Arq. brasil. de oftal. **20**:473-485, 1957.

Over 12,000 ophthalmic operations were performed in a seven-year period in a hospital in Campinas, Brazil. About 2,300 patients had general anesthesia for the surgery; some form of local anesthesia was given for the others. Among the factors which influence the choice of anesthetic are the age of the patient, the type of procedure to be done, the mental status of the patient, and the presence or absence of inflammation. There is a certain risk associated with general anesthesia, and the value of the recovery room is stressed. Complications may occur with both types and are briefly reviewed in the article. The additional use of curare, ataractic drugs and ganglioplegic agents singly or combined have been of great value in both types of anesthesia. (8 tables) James W. Brennan.

François, J., Neetens, A. and Collette, J. M. **Historadiography of the optic nerve. A preliminary report.** Bull. mém. Soc. franç. d'opht. **70**:411-421, 1957.

Microradiography provides radiologic pictures of a tissue section. Long-wave type of X rays are essential. In contradistinction to the classical microscopy, historadiography depends on the difference of wave absorption in the diverse constituents of an organ. Nervous tissue, for example, is permeable to even very soft X rays and therefore causes dark depositions. Connective tissue is much more opaque, more so if it contains many elastic fibers and the deposition is much clearer. Pigment granules are, strangely, very penetrable to X rays, whereas bone structures resemble the pictures achieved by the old technique. The apparatus itself and details of the techniques, the preparations as well as the interpretations of the pictures are discussed. The present study deals with a normal optic nerve with special emphasis on the interfascicular structures, so important in abnormal situations and difficult to interpret with the methods at hand. Another advantage of historadiology is the potential investigation of thick slides and consequently a better spatial reconstruction. (10 figures) Alice R. Deutsch.

Gallois, Jean. **Methods to induce improvement of visual acuity and myopia gravis.** Bull. mém. Soc. franç. d'opht. **70**: 381-387, 1957.

"La survision provoquee" is a more or less physiologic phenomenon of temporary visual improvement by vasodilatation and diverse metabolic influences. It has been investigated and interpreted by the author predominantly in patients with cataract and vascular abnormalities of the retina. The present paper includes

a report on 113 high myopes who were treated with various kinds of vasodilators. The variations in refraction and in visual acuity are summarized. The effect of vasodilators on ocular circulation and the inter-relationship of pupillary diameter, stage of adaptation, and potential psychologic factors are also discussed.

Alice R. Deutsch.

Klein, M. **A new keratoscope—with self-luminous Placido disc.** Brit. J. Ophth. **42**:380-381, June, 1958.

A miniature Placido disc has been incorporated into the plastic head of a small battery-in-handle instrument, thus creating a practical, noncumbersome instrument for examination of the cornea. This keratoscope head is made to fit the Keeler "New Era" ophthalmoscope handle. (1 photograph) Lawrence L. Garner.

Korchmáros, I. **Control of the magnetic test by ophthalmoscopy in cases of intraocular foreign bodies.** Szemeszet **2**:69-70, 1958.

The author describes 27 cases in which the magnetic test of intraocular foreign bodies was controlled by ophthalmoscopy. If the foreign body is magnetic it shows a slow movement during the magnetic test. It is proposed to apply this harmless procedure whenever an intraocular foreign body is visible or suspected with the unaided eye or by ophthalmoscopy. If the test is positive (the foreign body makes a move) then magnetic operation is required; if the test is negative then the magnetic operation is of no use and the opening of the globe is avoidable. Gyula Lugossy.

Lee, D. J. **A delayed diagnosis of bung eye.** M. J. Australia **1**:743, May 31, 1958.

Septoconopus stygius is a diurnally active blood-sucking fly with a peak abundance in November. It is distributed over a wide area of coastal New South Wales. It attacks man, animals, and birds. The bites are painless and if they occur in the region of the eye they are likely to cause acute edema of the lids. (2 references)

Ronald Lowe.

Maurice, D. M. **A recording tonometer.** Brit. J. Ophth. **42**:321-335, June, 1958.

The details of a new instrument for tonography are described; its advantages are 1. that the patient can be up and about or change his position without disturbing the device clamped to his head, and 2. its greater accuracy. It is primarily a tool for research and far too complicated for consideration as a clinical instrument. Eyes of normal subjects and cadavers have been tested and a future report dealing with glaucoma subjects is to follow. (14 figures, 2 references)

Lawrence L. Garner.

Mead, K. W. and Robertson, D. F. **Radiation therapy in certain eye conditions.** Tr. Coll. Radiol. Australasia **1**:83-87, 1957.

The authors discuss different sources of ionizing radiation and favor a strontium—90 place. The lesion is outlined by a ring applicator into which the plate is placed. The plate is bevelled to fit the eye. The following conditions have been treated: 1. epithelioma of the limbus, 2. recurrent pterygium, 3. vascularizing lesions of the cornea, 4. Mooren's ulcer, and 5. vernal conjunctivitis.

For lesions on the cornea or sclera single-dose applications are advised because these tissues do not recover quickly enough to benefit from fractionation. Pterygia should be excised rather than transplanted because much β-ray dose is wasted in penetrating thickened tissue.

Ronald Lowe.

Mueller, H. K. **The physical basis of ophthalmodynamometry.** Arch. chil. de oftal. **39**:87-91, July-Dec., 1957.

The author describes the fundamentals of ophthalmodynamometry, concluding that the measurements obtained with this method are of the pressures halfway between the origin of the central retinal artery and the artery at the disc. Alterations in the measurements obtained will occur in cases of arteriolar constriction or of venous engorgement and a value plus or minus 7 mm. from the formula has pathologic significance. The author believes that the pressure in the central retinal artery is about 0.475 times the humeral pressure.

This diagnostic method is especially valuable when an evaluation of drugs acting on the cerebral vascular system is desired. (2 figures) Walter Mayer.

Réthy, I. **A new type of trial frame for spectacles prescription.** Szemeszet **2**:88-89, 1958.

Réthy describes a simple plastic trial frame without bows and with a Maddox disc and an obturator to be turned alternately before each of the eyes.

Gyula Lugossy.

Rodger, F. C. **Eye diseases in African children—with special reference to onchocerciasis and malnutrition.** Brit. J. Ophth. **42**:336-347, June, 1958.

In an extensive survey of African children the common causes of blindness were found to appear in the following order of frequence: 1. trachoma, 2. measles, 3. smallpox, 4. keratomalacia, and 5. phlyctenulosis. In heavily infested areas where the disease is endemic three percent of the children were found to have ocular onchocerciasis. Vitamin A deficiency produced a characteristic type of keratomalacia in children with a painless and symptom-free iris prolapse without evidence of an inflammatory reaction. Another interesting finding was a triad of signs which was much more indicative of a diagnosis than are Bitot's spots. This triad consisted of a gathering of whipped clear mucus in the outer canthus, conjunctival pigmentation adjacent to the limbus, and folds in the bulbar conjunctiva. (6 figures, 2 tables, 7 references)

Lawrence L. Garner.

Viallefont, H., Boudet, C., Billet, B. and Costeou, J. **Arterial retinal pressure and intraocular tension during "Sakel's treatment."** Bull. mém. Soc. franç. d'opht. **70**: 368-380, 1957.

The effect of insulin shock on humeral and retinal arterial pressure and on ocular tension has been investigated systematically several years ago by Streiff and his associates. The present study concerns 52 schizophrenic males and females, 25 to 35 years of age. There was a remarkable discordance in the findings of this group of co-workers; Cossa found a constant elevation of the retinal arterial pressure while for Viallefont a depression was the rule. Variations in the reaction of various patients towards insulin and variations in the time of reading in reference to a specific level of the coma were given as reasons for these discrepancies. The fluctuations of the ocular tension were not essential; a mild tendency towards a lowering of the tension was seen during the coma. In spite of the high doses of insulin, up to 10,000 units in a three months' period, only temporary engorgements of retinal vessels and temporary blurring of the nerve heads were found on ophthalmoscopic examination. Nevertheless, the possible hazards connected with this therapy limit its use to individuals who are physiologically young with a healthy cardiovascular system. (2 figures, 2 curves)

Alice R. Deutsch.

Vörösmarthy, D. and Benko, K. **Solar cautery.** Szemeszet **95**:5-7, 1958.

An apparatus called "solar cautery" by the authors is described. It is suitable for

intraocular interventions by the use of sunshine. The advantages of this apparatus over the direct use of sunshine are the shorter exposure time, and in the possibility of performing the coagulation under direct visual control. Satisfactory results have been obtained with this apparatus in experiments on rabbits' eyes.

Gyula Lugossy.

Wynne Parry, T. G. **New design in anterior chamber lenses.** Brit. J. Ophth. **42**:376-379, June, 1958.

A new type of anterior chamber lens is described which is designed to avoid some of the drawbacks of the Strampelli lens. The present lens is a plastic lenticulus held in a small tantalum frame of two arms. This new type of lens is designed to prevent pressure at the angle, to be easily inserted and removed if necessary and to avoid the necessity of multiple lenses in order to obtain a good fit.

Lawrence L. Garner.

7

CONJUNCTIVA, CORNEA, SCLERA

Alberth, B. **Therapeutic keratoplasty.** Szemeszet **95**:12-18, 1958.

The literature of therapeutic keratoplasty is reviewed. On the basis of eight cases, the author outlines the indications for surgical intervention, the probable results, and the most useful methods of operation. The author favors the Harms uninterrupted corneal suture.

Gyula Lugossy.

Alimuddin, M. **Incidence and treatment of trachoma in Pakistan.** Brit. J. Ophth. **42**:360-366, June, 1958.

In an attempt to estimate the trachoma incidence by reviewing the out-patient records of the ophthalmological clinics over a five-year period the author gathered the following data: 1. 53 percent of the population was found to have trachoma in some stage, 2. the commonest age of onset was two to five years, 3. trachoma accounts for 0.08 percent of the 100,000 estimated blind, 4. females were involved twice as frequently as males and suffered more severely from this disease, 5. the condition usually increased during the hot seasons, and 6. trachoma complications were found in 24 percent of the patients examined. (2 figures, 3 tables, 10 references) Lawrence L. Garner.

Ayala Haedo, A., Boggino, J. and Mercado, M. **A case of conjunctival paracoccidiodosis.** Arq. brasil. de oftal. **20**: 450-457, 1957.

A man, 53 years of age, had a swelling of the upper lid for five months and an ulcerated lesion of the conjunctiva near the ciliary border giving the clinical appearance of blastomycosis. A biopsy specimen led to a diagnosis of paracoccidiodosis. Systemic administration of sulfadiazine was apparently unsuccessful and the patient soon died. (8 photomicrographs) James W. Brennan.

Bietti, G. B. and Lanzieri, M. **The use of a sulfamide derivate with delayed elimination for the treatment of trachoma.** Rev. intern. du trachome **34**:270-287, 1957.

A new sulfonamide, sulfamethoxypyridazine (Kynex, Lederle), with the advantage of delayed elimination, was tried by the authors in 57 patients, mostly children of school age, with second stage trachoma. No side effects were noted and 70 percent of cures obtained. Eight to twelve ctgs. per kg. of body weight was administered during three months. (2 figures, 2 tables) Jose A. Ferreira.

De Rezende, Cyro. **The use of corneal acrylic prostheses.** Arq. brasil. de oftal. **20**:425-449, 1957.

Observations on the success of the Ridley and Strapelli acrylic lenses and the experiences gained during the war

have led to the experimental use of acrylic corneal implants. The author has followed the technique of Legrand in a series of animal experiments and proposes several of his own modifications. He presents case histories of four patients operated on by this technique, but feels the follow-up period to be too short to draw any conclusions. He makes a 4 mm. trephine incision with a lamellar keratectomy of about one-third of the corneal thickness. This is followed by the preparation of a sulcus in the corneal parenchyma around the orifice of the trepanation, and should be large enough to receive the prosthesis. A vertical corneal incision, preferably on the temporal side, is made with a cataract knife, and a spatula is passed, forming a tunnel with the previously made sulcus. The trephine is reapplied and the site is converted to a perforating keratectomy. The acrylic prosthesis is now passed through the corneal incision and positioned in the sulcus. (22 figures, 15 references)

James W. Brennan.

d'Haussy, R. and Rit, J.-M. **Trachoma in French West Africa.** Rev. intern. du trachome **34**:297-310, 1957.

The authors remark on certain points of interest in a thorough survey in relation to trachoma in French West Africa. More than three million people were examined. Contamination was found in 4.33 percent, with an unequal geographic distribution. It seems to have a spontaneous cicatrization and the measures to fight trachoma should favor it. (1 figure, 1 table, 13 references)

Jose A. Ferreira.

Litricin, O. and Radovanovic, M. **Differential diagnosis between trachoma and folliculosis.** Rev. intern. du trachoma **34**: 349-354, 1957.

Cortisone cannot be used for the differential diagnosis of early trachoma from folliculosis because it worsens many cases of folliculosis. The pathologic picture does not differentiate doubtful cases of trachoma from folliculosis. Aureomycin does not cure folliculosis so it should not be used in borderline cases until the diagnosis of trachoma has been made certain. (2 tables, 9 references)

Jose A. Ferreira.

Malnou. **Importance of trachoma as a cause of blindness in South Tunisia.** Rev. intern. du trachome **34**:322-335, 1957.

Trachoma accounts for 45 percent of the blindness in South Tunisia including that which was the result, directly or indirectly, of infections of the lacrymal system, trichiasis, corneal anesthesia, and so on. Although the relation has not been clearly established, glaucoma is by far more common (35 percent) in trachomatous patients. Accidental and surgical trauma to the eye is considerably complicated by the presence of trachoma.

Jose A. Ferreira.

Merz, E. H. and Walsh, J. J. **Tuberculosis of the external eye.** Illinois M. J. **113**:238-239, May, 1958.

The authors present a case of ulcerative tuberculosis of the conjunctiva secondary to active pulmonary tuberculosis. The ulceration responded to local and systemic antitubercle drugs, just before the patient died. (1 figure, 14 references)

Irwin E. Gaynon.

Pajor, J. **Posterior scleritis.** Szemeszet **2**:74-75, 1958.

The case of a 12-year-old girl is described. The symptoms were: pain, protrusion, detachment of the retina, and impairment of vision; the diagnosis, posterior scleritis. Full recovery followed the oral administration of salicylates.

Gyula Lugossy.

Poleff, L. **Insufficiency of the methods against trachoma. Outlook for the future.** Rev. intern. du trachome **34**:355-363, 1957.

The author finds that the present sulfamide and antibiotic therapy against trachoma in large groups of population is insufficient. Although international organization and coordination of research are on the way, studies on immunotherapy for the purpose of finding a specific vaccine should be favored. (27 references) Jose A. Ferreira.

Rohrschneider, W. **Trachoma in Germany.** Rev. intern. du trachome **34**:288-296, 1957.

After the migration of 400,000 people of German blood from trachomatous countries of oriental Europe, no infection of the autochthonous Germans appeared. About 12,000 trachomatous individuals have been included in the German community and there has been no subsequent complication, a fact which emphasizes the high general and individual hygiene in Germany. (1 figure, 1 table, 16 references) Jose A. Ferreira.

8

UVEA, SYMPATHETIC DISEASE, AQUEOUS

V. Sztanojevits, A. **Successful early intervention on a postoperative implantation iris cyst.** Szemeszet **95**:19-21, 1958.

This is the description of an implantation cyst of the iris, diagnosed the sixteenth day after the operation and easily removed three days later. The histologic picture is described. Gyula Lugossy.

Vörösmarthy, D. and Pénzes, T. **Sphincterotomy by means of "solar cautery."** Szemeszet **2**:71-73, 1958.

The first application of direct solar coagulation (Kettesy) to the human iris is described. The successful procedure was carried out on a patient with aphakia. The visual acuity improved from 0.02 to 0.2. Full details are given.

Gyula Lugossy.

9

GLAUCOMA AND OCULAR TENSION

Algan, B. **Study on the heredity of congenital glaucoma.** Bull. mém. Soc. franç. d'opht. **70**:436-445, 1957.

Hereditary factors have been recognized in the etiology of congenital glaucoma by most authors, in spite of the fact that the genetic nature of this serious disease has been quite controversial only a few years ago. The mode of transmission, however, has not been established.

The history of a couple, both partners blind from congenital glaucoma, is discussed. Their children, one boy and one girl, also had congenital glaucoma. These unusual cases and the pedigree of the two families prove to be a significant contribution toward a better understanding of the problem of heredity but do not clarify completely the question of the mode of transmission (5 figures, 41 references) Alice R. Deutsch.

Arentsen, J., Bitran, D. and Barrientos, E. **Tension curves in chronic simple glaucoma.** Arch. chil. de oftal. **39**:135-144, July-Dec., 1957.

The authors discuss the importance of routine tonometric examinations in all patients above 40 years of age; in their practice all patients with a tension between 23 and 30 mm. are referred to the glaucoma service. There it is sometimes necessary to take tension curves as the only method of diagnosis of glaucoma. Among 55 patients in whom curves were taken, they were found to be positive in 52. The hour of greatest tension was at 8 P.M. in the majority of the cases. (8 graphs, 7 tables) Walter Mayer.

De Carvalho, Celso A. **Gonioscopy and tonography in the surgical treatment of primary glaucoma.** Rev. brasil. oftal. **17**: 113-122, March, 1958.

The author reviews the anatomic find-

ings in gonioscopy and summarizes briefly the findings in acute and chronic glaucoma. He outlines the knowledge basic to tonography, as applied to acute and chronic glaucoma and reviews the different surgical techniques available in primary glaucoma which may be chosen after consideration of the gonioscopic and tonographic findings. (21 references)

Walter Mayer.

Ferraris de Gaspare, P. F. **Antiglaucomatous operations in eyes with healed trachoma.** Rev. intern. du trachome **34**: 320-321, 1957.

The author reports 29 Elliot, 12 Lagrange, 8 Foroni operations, 14 iridencleises, 9 cyclodialyses and 12 iridectomies done on trachomatous patients ill from two to six years. Poor results followed operation by the Elliot, Foroni or Lagrange methods, better results were noted after iridencleisis.

Jose A. Ferreira.

Ferreira, Luiz E. **Technical details of iridencleisis.** Rev. brasil oftal. 17:137-142, March, 1958.

The author describes his technique for iridencleisis which differs from that generally used in that the author outlines the anterior chamber limits by Minsky's maneuver. Having the assistant direct a light on the limbus inferiorly, he can see clearly outlined the demarcation of the chamber superiorly, where he enters by an ab externo incission with an Elschnig knife. (6 figures) Walter Mayer.

Fonseca Caldeira, Jorge Alberto. **Provocative tests in glaucoma.** Rev. brasil. oftal. 17:103-110, March, 1958.

The author describes several tests: jugular compression test, lability test, cafeine, homatropine, priscol, vascular, postural and bulbar pressure tests. An evaluation is made of their significance. (4 references) Author's summary.

Gruterich, E. and Cunha, S. L. **Mode of action of the drugs used in the treatment of primary glaucoma.** Rev. brasil. oftal. 17:123-134, March, 1958.

The author reviews briefly the pharmacologic actions of the different types of drugs—sympathomimetics, sympatholitics, and parasympathomimetics—used in the treatment of glaucoma. He deals extensively with the mode of action of Diamox and concludes the article by mentioning the drugs which act on the corticodiencephalic centers. (51 references) Walter Mayer.

Kornzweig, A. L., Sugar, H. S., Ballentine, E. J., Barrenechia, S., De Toledo, R. and Belfort-Mattos, R., Boado, L. A., and Anton, M. **Symposium: Glaucoma.** Trans. Fifth PanAm. Cong. Ophth. Santiago. 1: 147-241, 1956.

Kornzweig, A. L. **Pathology of the angle.** pp. 147-158.

Microscopic sections of 11 eyes from patients aged 65 to 90 years of age and affected with primary glaucoma treated only by medical means, revealed alterations of the lumen of Schlemm's canal varying from simple narrowing to total occlusion, thickening and sclerosis of the trabeculae, pigment migration into the intertrabecular spaces, and endothelial proliferation. The question arises whether these changes are the cause or the result of increased intraocular pressure. (17 photomicrographs, 20 references)

Sugar, H. S. **Gonicscopy.** pp. 159-162.

The value of gonioscopy in glaucoma is emphasized through its applications for 1. differential diagnosis of certain types of glaucoma, 2. preoperative selection of surgical approach in cases requiring either iridectomy or filtering operation, 3. determination of the patency of the cleft in cyclodialisis, and 4. accurate determination of the causes of failure in trephine operations in which the opening

may be blocked by the iris, lens, ciliary processes or conjunctival scarring. Another valuable indication is the detection of goniosynechias which are present in acute or subacute inflammatory conditions of the angle.

Ballentine, E. J. **Tonography.** pp. 163-171.

The author offers a concise presentation of the physiologic and mathematical aspects involved in the determination of the "facility of outflow", represented by "C", as originally presented by W. Morton Grant. Practical application for this method requiring relatively simple instrumentation is seen in the management of glaucoma with miotics, where a low "C" value associated with normal I.O.P. indicates repeated study of the visual fields and increase in the strength or the frequency of the miotic agents. Finally, the value of tonography in diversified aspects of the glaucoma problem is outlined. (1 figure, 14 references)

Barrenechea, Santiago. **Provocative tests.** pp. 173-199.

The author insists on the undoubted importance of provocative tests in the early diagnosis of chronic simple glaucoma, in spite of their frequent unreliability and the apparently paradoxic reactions observed in some cases. He uses them with an "'analytical" point of view, that is to say, trying to find out by a definite test, which ocular structure or structures are inadequate, obtaining in such manner functional information and not merely "statistical" conclusions furnished by an undiscriminating use of tests. He goes over the data referring to normal and pathologic ocular tension and to their spontaneous phasic variations, and considers their detailed knowledge utterly necessary for a better interpretation of provocative tests. He describes the most frequently used tests and results obtained by W. Leydhecker, W. Rohrschneider, and others. (2 tables, 104 references)

De Toledo, Renato and Belfort-Mattos, Rubens, **Visual fields.** pp. 201-207.

The determination of the visual field is still the safest way of making an early diagnosis and of assessing the evolution in glaucoma patients. In these last few years studies of flicker fusion perimetry have revealed its importance in glaucoma. Even though it is an old method—it had been investigated by Markow as early as 1901—it has been systematised only recently by Phillips, Weekers, Roussel and Miles, who claim its propedeutic usefulness in several affections besides glaucoma.

Flicker perimetry defects appear early in glaucoma and are generally more evident than the defects revealed by standard campimetry. Critical flicker frequency in glaucoma is generally lower in the more involved sector of the visual field.

Boado, Luis Alberto. **Medical treatment.** pp. 209-235.

A pharmacodynamic analysis of the currently used drugs is presented. Diamox, by reducing the amount of aqueous secreted by the ciliary body is valuable in primary glaucoma. In secondary glaucoma Diamox is inhibited after several weeks of treatment, probably because of a sub-clinical acidosis and the eye becomes temporarily refractory to this therapy. The use of Diamox in secondary glaucomas is enhanced by the use of miotics and also by steroids when these are indicated. Few new developments of therapy with the miotic drugs have been reported; the best combination seems to be Diamox with one colinergic agent (pilocarpine) and with one cholinesterasic agent (physostigmine).

ACTH has been proven ineffective, while progesterone acts by blocking the hypertensive action of foliculine. This is a promising field for the study of glau-

comatous ethiology and therapy in women during the menopause or in cases of ovarian dysfunction associated with glaucoma. (2 tables, 32 references)

Anton, Manuel. **Surgical treatment.** pp. 237-241.

In chronic simple glaucoma, surgery is advisable when there is progressive resistance of the disease to medicinal therapy, when this therapy cannot be administered at home, and when the patient cannot present himself for regular ophthalmic control. When surgical intervention has been decided upon, the following factors should be determined: 1. volume of aqueous humor production (through the fluorometric method of Goldmann-Weekers), 2. resistance of aqueous humor excretion by tonography (Grant) and the bulbar pressure test (Blaxter), 3. gonioscopic examination which may indicate the best place to make surgical drainage when anterior synechias are present, 4. determination of the basic tension curve, and 5. the rigidity of the sclera should be studied.

In surgery of chronic simple glaucoma, both in narrow and open angles, preference is given to fistulising operations. When treating Negroes the author prefers iridencleisis when the iris is not atrophic and specially when the basic tensional curve is not very high. He prefers Elliot trephining in all other cases for its highly hypotonising action when the optic nerve has been excavated by glaucoma, because a tension which should be considered normal in an eye with glaucomatous cupping, might be lower than the tension the same eye presented before being affected with glaucoma. Comparative statistical data are given of both fistulating operations. (1 table)

Gustavo Scioville-Samper.

Maumenee, A. E., Manzitti, E., and Bertotto, E. V. **Symposium: Infantile Glaucoma.** Trans. Fifth Pan Am. Cong. Ophth. Santiago 1:247-267, 1956.

Maumenee, A. Edward. **Gonioscopy.** pp. 247-252.

The gonioscopic findings in normal infant eyes and in eyes with congenital glaucoma differ from those in adult eyes. In normal infant eyes the trabeculae are more translucent, iris processes are more prominent, and the iris inserts into the ciliary body nearer the scleral spur. In eyes with congenital glaucoma there is an insertion of the root of the iris into the trabeculae, Schlemm's canal is almost invariably present and in eyes with a relatively low tension can be demonstrated by jugular pressure, and an actual "membrane" is not present over the angle.

The histologic findings in normal infant eyes and in eyes with congenital glaucoma are described. The most consistent pathologic finding is an abnormal insertion of the iris into the trabeculae. The influence of this in the pathogenesis of congenital glaucoma is discussed. (6 references)

Manzitti, Eduardo. **Signs.** pp. 253-259.

Congenital glaucoma and hydrophthalmia or buphthalmia, have a pathologic substratum: a developmental anomaly at the chamber angle. Such disgenesis of the angle can be recognized in gonioscopy by the persistence of embryonic mesodermic tissue, and the absence of Schlemm's canal. The other principal manifestation is a full or partial gigantism of the eye, that is manifest in increased diameters of cornea and globe and deepening of the chamber. There are clinical forms without ocular hypertension which in several cases have been wrongly diagnosed as megalocornea.

Bertotto, Enrique V. **Treatment.** pp. 261-267.

The author points out the inherent difficulties of this subject such as scarcity of cases and a proper follow-up over the years. Medical treatment is of no avail. Gonioscopic examination and tonometry should be done in the immediate pre-

operative stage both as an indication for the surgical approach and as a basis line for functional evaluation. Early surgical treatment is indicated in all cases to avoid closure of Schlemm's canal, injury to the optic nerve and distension of the globe. The prognosis is best when surgery is performed early after onset of symptoms. The different surgical techniques in use today—Elliot's trephine, iridencleisis, goniotomy, cyclodialysis and cyclodiathermy are discussed. An analysis of Barkan's operation, including its advantages, indications, technique and difficulties is followed by a summary of his 17 years' experience with it.

Gustavo Scioville-Samper.

10

CRYSTALLINE LENS

Carli, J. and Autric, C. **Preoperative subconjunctival injection of penicillin and postoperative systemic antibiotic therapy after extraction of senile cataract.** Ann. d'ocul. **191**:297-299, April, 1958.

The authors, who work in Tunisia, state that about 40 percent of their patients with senile cataract show evidence of trachoma. In this group postoperative infections appear to be more frequent. They therefore instituted the preoperative subconjunctival injection of 30,000 units of penicillin and the postoperative systemic administration of 500,000 units of penicillin and one gram of dehydrostreptomycin for five days. Since the introduction of this procedure they have performed 150 cataract extractions without a postoperative infection. David Shoch.

Costa Fernandes, Ruy. **Recent developments in the surgery of cataract.** Arq. brasil. de oftal. **20**:458-472, 1957.

The author reviews the current literature on the surgical treatment of cataract and presents an extensive bibliography. The preoperative preparation, anesthesia, the technique of extraction, and the complications are all discussed. The acrylic lens of Ridley and the Strampelli lens are compared. Although the latter seems irritating to the iris and a possible source of trauma to the chamber angle, the incidence of complications and visual results compare favorably with those of the Ridley implant. (55 references)

James W. Brennan.

Sédan, Jean. **Cataract extraction by the Smith method in a case of megalocornea.** Ann. d'ocul. **191**:286-292, April, 1958.

The author describes a cataract extraction performed on a patient with megalocornea. A Smith extraction was planned but at the moment of application of the hook in the six-o'clock position, the superior pole of the lens presented itself in the wound. Delivery was uneventful and without loss of vitreous. The final visual result was 20/30. As a result of this observation the author feels that perhaps this is a superior method of cataract extraction in cases of megalocornea. (57 references) David Shoch.

11

RETINA AND VITREOUS

Dejean, C. **Circulation disturbances in the fetal retina and vitreous preceding fibroplastic changes.** Bull. mém. Soc. franç. d'opht. **70**:357-367, 1957.

After a short review of the concepts related to the progression and regression of the fetal intraocular vascular system, the author discusses his own ideas on retrolental fibroplasia. He agrees with other workers that the fibroplasia of prematurity is an essentially vascular affection and that the first manifestations occur in the equatorial region. It is known that in this area, previously occupied by the primary vitreous, vascular remnants containing blood through the seventh and eighth fetal months provide

a communication with the anterior vascular network supplying the iris and choroid. Excess of oxygen seems to be especially damaging to this group of vessels. They are still permeable at this period but in a stage of regression and therefore inclined to excessive hypertrophy in response to any stimulation. At this specific period the retinal vascular tree is still very delicate, the ora serrata and surroundings practically devoid of vessels and it would be difficult to explain how those vessels could be the origin of the basic angiomatosis. This angiomatosis should be ascribed primarily to the rests of the vascular fetal sheath and only in the third stage when the retina is already partly detached to the retinal vascular system. This theory is apparently supported by the pathologic findings in an eye with many congenital deformities as well as hyperplastic primary vitreous. The characteristic structure of the primary vitreous fibers becomes interspersed with a dense mass of fibrous tissue, newformed vessels, proliferated epithelium, and cartilage. As the vitreous itself could not have produced this connective tissue it had to be a derivative of the vessel wall. The origin and pathogenesis of retrolental fibroplasia is then interpreted in accordance with these findings. (10 figures)

Alice R. Deutsch.

François, J. and de Rouck, A. **Use of electro-retino-encephalography in the differential diagnosis of tapeto-retinal degenerations.** Ann. d'ocul. **191**:258-285, April, 1958.

In order to record the electrical response of the eye to light stimulation the authors employ three types of illumination. First a standard white light, second a neon lamp which has primarily an orange color and third a xenon lamp which gives off a blue light. At the same time they make an encephalographic tracing. Using these techniques they have investigated a group of degenerations of both the peripheral and central retina. In the first group are included retinitis pigmentosa, retinitis punctata albescens, gyrate atrophy of Fuchs, and choroideremia. The central group consists of macular degeneration of Stargardt, central pigmentary degeneration, amaurotic idiocy, Sorsby's inflammatory dystrophy, angioid streaks, and senile macular degenerations.

In the peripheral degenerations the retinal response to light is absent or markedly reduced, conduction is slowed and the electro-encephalogram shows diffuse changes. The central degenerations show similar changes to a much lesser degree. However, in senile macular degeneration there is no electro-encephalographic disturbance. All other degenerations apparently have a hereditary defect in the development of the prosencephalon. (17 figures, 58 references)

David Shoch.

Lijó Pavía, Justo. **Stereoretinotopography. Rev.** oto-neuro-oftal. **33**:7-8, Jan.-March, 1958.

The author comments on a paper published by Sedan and his collaborators on the superiority of binocular vision as compared with monocular vision, a superiority which has not been completely explained. Several years ago he noted this superiority of binocular vision when labeling some retinograms for publication. Lines and letters placed on the retinogram would have taken away some of the clarity so that the author devised the method of presenting two identical retinograms, labeled one of them and viewed them binocularly. The two pictures became superimposed and the labeling was clear.

Walter Mayer.

NEWS ITEMS

EDITED BY DONALD J. LYLE, M.D.
411 Oak Street, Cincinnati 19, Ohio

News items should reach the editor by the 10th of the month. For adequate publicity, notice of postgraduate courses and meetings should be received three months in advance.

DEATHS

Dr. Edward Philip Drescher, Berkeley, California, died July 12, 1958, aged 43 years.

Dr. Samuel Engel, San Francisco, California, died June 28, 1958, aged 59 years.

Dr. Jaroslav H. Hulka, Long Island City, New York, died June 18, 1958, aged 64 years.

ANNOUNCEMENTS

CALL FOR PAPERS

The 1959 meeting of the Section on Ophthalmology, American Medical Association, will be held in Atlantic City, June 8 to 12, 1959.

Anyone wishing to present a paper before the Section is urged to communicate with Dr. Harold G. Scheie as soon as possible. A title and abstract of 50 to 150 words must be in his hands by January 1, 1959. Anyone wishing to present a scientific exhibit should contact Dr. Frank W. Newell as soon as possible.

A $250.00 prize is offered for the best paper and another $250.00 prize for the best scientific exhibit prepared for the Section on Ophthalmology at each Scientific Session.

Frank W. Newell, M.D., Representative to Scientific Exhibit, 950 East 59th Street, Chicago 37, Illinois.

Harold G. Scheie, M.D., Secretary, Section on Ophthalmology, 313 South 17th Street, Philadelphia 3, Pennsylvania.

POSTGRADUATE COURSE

The Department of Ophthalmology of the State University of New York Upstate Medical Center at Syracuse will present its ninth annual postgraduate course in ophthalmology at the Hotel Syracuse, Friday and Saturday, December 5 and 6, 1958. The following lecturers will participate: Dr. John H. Dunnington, Dr. A. Edward Maumenee, and Dr. George K. Smelser.

The tuition fee is $25.00, payable to the State University of New York Upstate Medical Center at Syracuse, 766 Irving Avenue, Syracuse 10, New York. This fee covers tuition, daily luncheons, and dinner on Friday night. The course will be limited to 60 members. These will be accepted in the order in which applications, accompanied by checks, are received. Inquiries regarding the course may be addressed to James L. McGraw, M.D., at the same address.

COURSES FOR OPHTHALMOLOGISTS

New York University-Bellevue Medical Center Post-Graduate Medical School announces the following courses for ophthalmologists:

Ophthalmic plastic surgery (for specialists). A part-time course of five days' duration, 2:00 to 5:00 P.M., November 17th through 21st. Covers the essentials of ophthalmic plastic surgery for the practicing ophthalmologist. Special emphasis is laid on the more common fundamental procedures peculiar to lid surgery. Instruction is by lecture and demonstration. The steps in the various techniques are systematically outlined and the choice of the suitable technique for various clinical conditions is considered. Given under the direction of Dr. Sidney A. Fox.

Surgery of the cornea. A full-time course of five days' duration, December 1st through 5th. Designed to offer thorough coverage of current concepts and practices in the field of corneal surgery. Afternoons from 2:00 to 5:00 P.M. are devoted to didactic lectures, illustrated by lantern slides and motion pictures. During the mornings, as patient material is available, opportunity is offered to observe surgical procedures in the operating room. On the last morning of the course, students perform surgical procedures on animal eyes. Given under the direction of Dr. Ramon Castroviejo.

Neuro-ophthalmology. A part-time course of five days' duration, 9:00 A.M. to 12:00 M., January 19 through 23, 1959. Consists of a review of the anatomy of the nerve fibers, instrumental and non-instrumental perimetry, classification and significance of field defects, types of oculomotor and optic atrophy, chiasmal syndromes, and pupillary reactions. Discussion of the types of abducens palsy, diverse forms of gaze palsy (supranuclear palsy) nystagmus, and convergence disturbances. A short review of cerebro-ocular diseases and functional disturbances of the eye is given. This course is under the direction of Dr. Alfred Kestenbaum.

For further information, write:

Office of the Associate Dean
New York University Post-Graduate Medical School
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New York 16, New York

NEW ORLEANS ACADEMY

The annual midwinter convention of the New

Orleans Academy of Ophthalmology, to be held in New Orleans, February 23 through 27, 1959, will feature a symposium on "Diseases and surgery of the retina." On the panel will be Dr. Arthur J. Bedell, Dr. Harold F. Falls, Dr. Bertha A. Klien, Dr. Dohrmann K. Pischell, Dr. C. Wilbur Rucker, Dr. Charles L. Schepens, Dr. Donald M. Shafer, and Dr. Lorenz E. Zimmerman. Hotel reservations should be made early by writing to the Executive Secretary, P.O. Box 469, New Orleans 1, Louisiana.

Miscellaneous

Afro-Asian congress

Trachoma was one of the main subjects of study at the first Afro-Asian congress of ophthalmology, held in Cairo in March. The question of trachoma Stage IV was discussed and it was unanimously decided that this stage of trachoma should be omitted from all classifications of trachoma. Some of the reasons for this decision are:

1. It is universally agreed that when trachoma heals completely, the condition is called trachoma 4. So trachoma 4 is a condition in which the patient is completely cured, is noninfectious, and has no trachoma, and it is ridiculous to consider such a condition as one of the stages of the disease.

2. Trachoma 4 is a great source of inexactitude and confusion as far as statistics, local or international, are concerned.

3. If a cicatrized lid should be given a name let it be called a "cicatrized lid."

For all these reasons, the first Afro-Asian congress of ophthalmology, comprising members from Ceylon, China, India, Indonesia, Iraq, Japan, Jordan, Lebanon, Philippine, Saudi Arabia, Soudan, Thailand, Tunis, Turkey, U.S.S.R. and The United Arab Republic (Egypt and Syria) resolved that trachoma Stage 4 should be omitted from all classifications of trachoma and that all concerned international organizations be so informed. (Sabri Kamel, M.D., general secretary, Cairo.)

Societies

Nassau meeting

The Nassau (county, New York) Ophthalmological Society met at Bay Shore, Long Island, on September 22nd. Instead of the regular scientific session, there was a discussion of local problems affecting ophthalmologists. The next meeting of the society will be on November 24th. Officers for the current year are: President, Dr. Harry McGrath; vice-president, Dr. Arthur E. Merz; secretary-treasurer, Dr. Jesse J. Michaelson; assistant secretary-treasurer, Dr. John R. Roche. Dr. Conrad Berens and Dr. Eugene T. Buckley are members of the council.

Central Illinois society

The 31st convention of the Central Illinois Society of Ophthalmology and Otolaryngology was held September 19th, 20th, and 21st at the Abraham Lincoln Hotel, Springfield. Guest speakers were Dr. Louis Joel Feit, New York, and Dr. I. D. Okamura, Boston. Dr. Louis R. Kent, Champaign, and Dr. Grover C. Otrich, Belleville, members of the society, also presented papers.

College of Surgeons

The clinical congress of the American College of Surgeons convened in Chicago, October 6th through 10th. At the ophthalmology session, there was a panel discussion of "Recent developments in ophthalmic surgery," with Dr. William B. Clark, New Orleans, acting as moderator. Leading the discussions were Dr. Lorand V. Johnson, Cleveland, "Orbit and lids"; Dr. R. Townley Paton, New York, "Corneal surgery"; Dr. F. Bruce Fralick, Ann Arbor, "Cataract and glaucoma"; and Dr. Albert D. Ruedemann, Detroit, "Surgery of the retina."

Personal

Dr. O. M. Duthie, Manchester, England, was elected master of the Oxford Ophthalmological Congress, succeeding Sir Tudor-Thomas.

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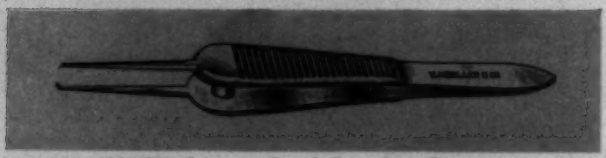

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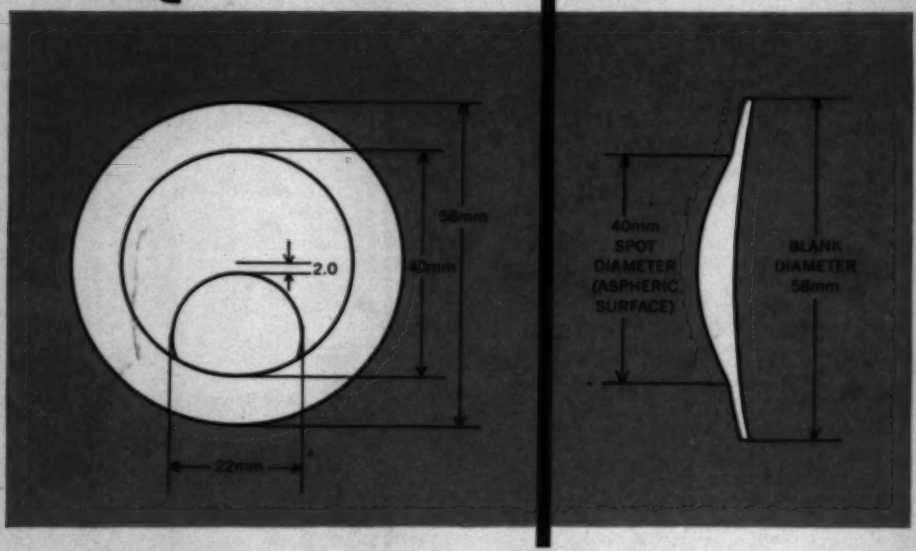

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